Serum total homocysteine concentrations in adolescent and adult Americans: results from the third National Health and Nutrition Examination Survey[1–4]

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ABSTRACT

Background: The elevation of circulating total homocysteine concentrations in a fasting state is associated with an increased risk of occlusive vascular disease.

Objective: The primary goals of this study were to describe the distribution of serum total homocysteine concentrations in the United States and to test for differences in homocysteine concentrations among sex, age, and race-ethnicity categories.

Design: Using surplus sera from phase 2 of the third National Health and Nutrition Examination Survey, we measured serum total homocysteine concentrations for a nationally representative sample of 3766 males and 4819 females aged ≥12 y.

Results: Age-adjusted geometric mean total homocysteine concentrations were 9.6 and 7.9 mmol/L in non-Hispanic white males and females, 9.8 and 8.2 mmol/L in non-Hispanic black males and females, and 9.4 and 7.4 mmol/L in Mexican American males and females, respectively. Age-adjusted geometric mean total homocysteine concentrations were significantly lower in females than in males in each race-ethnicity group ($P < 0.01$) and were significantly lower in Mexican American females than in non-Hispanic white and non-Hispanic black females ($P < 0.01$). There was a significant age-sex interaction ($P < 0.01$), reflecting the fact that homocysteine concentrations in females tended to diverge from those in males at younger ages and converge with those in males at older ages.

Conclusions: The first data on homocysteine concentrations in a nationally representative sample of Americans confirm the age and sex differences reported previously in nonrepresentative samples. These data also indicate that differences between Mexican American and non-Hispanic females may influence circulating homocysteine concentrations. *Am J Clin Nutr* 1999;69:482–9.

KEY WORDS Homocysteine concentrations, occlusive vascular disease, age, sex, race, ethnic groups, nutrition surveys, adolescents, adults, third National Health and Nutrition Examination Survey, NHANES III

INTRODUCTION

The elevation of total circulating homocysteine concentrations in a fasting state (fasting hyperhomocysteinemia) is associated with an increased risk of occlusive vascular disease (1–7) and increased mortality in individuals with previously diagnosed vascular disease (8). Each 5-μmol/L increment in total fasting homocysteine concentrations was shown to be associated with a 60–80% higher risk of coronary artery disease, a 50% higher risk of cerebrovascular disease, and a 6-fold higher risk of peripheral vascular disease (9).

Certain factors are related to total fasting homocysteine concentrations. Age and sex are 2 of its stronger determinants. Concentrations are higher in men than in women and at older ages (10–13). Menopausal status and estrogen replacement therapy appear to be related to fasting homocysteine concentrations in women (14–16). Elevated fasting homocysteine concentrations are associated with lower circulating concentrations and intakes of folate and vitamin B-12 (1, 10), and fasting hyperhomocysteinemia is also amenable to treatment with these vitamins (17–22).

Unlike the National Health and Nutrition Examination Surveys (NHANESs), which are designed to provide health and nutrition information on a representative sample of the noninstitutionalized, civilian US population (23), previous reports of circulating homocysteine concentrations in the United States were based on convenience samples or nonrepresentative population-based samples (2, 6, 10, 13). There is also little available information describing homocysteine concentrations in healthy adolescents and young adults and relating race and ethnicity to circulating homocysteine concentrations. In the present study,

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serum homocysteine concentrations were measured in sera from participants in phase 2 (1991–1994) of NHANES III. We present the distribution of serum homocysteine concentrations for adult and adolescent Americans by age, sex, and race or ethnicity. This study provides the first opportunity to describe total homocysteine concentrations in large samples from racial and ethnic minority groups and in healthy adolescents and young adults.

SUBJECTS AND METHODS

Subjects

NHANES III was designed to obtain nationally representative information on the health and nutritional status of the civilian, noninstitutionalized US population through interviews and direct physical examinations (23, 24). The survey began in the fall of 1988 and was completed in the fall of 1994. Approximately 40 000 persons were selected from 81 counties in 26 states. More than 36 000 persons were interviewed and >30 000 completed a standardized, detailed physical examination in specially equipped mobile examination centers.

The sampling scheme, which included persons aged ≥2 mo, was a stratified, multistage probability design with oversampling of young children (<5 y), older persons (>60 y), blacks, and Mexican Americans to allow more precise estimates of health and nutritional characteristics for these specific population subgroups. Other racial and ethnic groups, such as non-Mexican American Hispanics, American Indians, and Asian and Pacific Islanders, were included but were not oversampled. The survey was conducted in two 3-y phases and each phase was designed to provide nationally representative samples.

Total homocysteine concentrations were measured in surplus sera from phase 2 (1991–1994) of the NHANES III. The surplus serum samples were derived from a population sample of 13 635 males and females aged ≥12 y; 10 280 subjects were examined. Homocysteine data were missing for 16% of the participants for whom there were no surplus sera or from whom samples were not obtained at the survey examination. The prevalence of missing data was slightly greater in the group aged ≥80 y and in non-Hispanic whites. The protocol for measurement of homocysteine was approved by the Human Investigations Review Committee at the New England Medical Center.

Determination of serum homocysteine concentrations

Blood was drawn and processed in the mobile examination center under controlled, constant environmental conditions according to standard protocols (25). Participants had fasted for various lengths of time: 61% fasted for ≥8 h, 24% for ≥6–8 h, and 5% for ≥4–6 h. However, analyses showed that the length of the fast had no measurable effect on homocysteine concentrations. Whole blood, which was not treated with an anticoagulant, was collected into serum separator tubes and held at room temperature for 30–60 min before centrifugation at 115 × *g* for 15 min. Although total homocysteine in whole blood is artificially increased when held at room temperature because of continued production by red blood cells, the increase is minimal if the sample is centrifuged within 1 h of collection (26). Serum was separated, frozen at −20 °C, and transported on dry ice to the central laboratory of the Centers for Disease Control and Prevention for priority analyses. Samples went through 1–4 freeze-thaw cycles. It was shown previously that repeated freezing and thawing does not affect serum homocysteine concentrations (26). After priority analyses were completed, additional analyses were carried out subject to approval by the Surplus Sera Bank Steering Committee of the Centers for Disease Control and Prevention and National Center for Health Statistics.

The surplus serum samples were stored at −70 °C for 8 mo to 3 y before being analyzed for total homocysteine concentrations. Homocysteine was measured at the US Department of Agriculture Human Nutrition Research Center on Aging with the HPLC method of Araki and Sako (27). A single measure of homocysteine has been shown to reliably characterize a person's average, long-term homocysteine concentration (28).

Statistical analysis

We used sample weights in all analyses to account for unequal probability of selection and nonresponse and to produce estimates of means and percentiles that were representative of the noninstitutionalized, civilian US population. SUDAAN statistical software (29), which incorporates sample weights, was used to account for the complex survey design in the variance estimates. Because total homocysteine concentrations were extremely skewed, a logarithmic transformation was applied to these data to obtain the age-specific and age-adjusted geometric mean serum total homocysteine concentrations for males and females and for each racial or ethnic group. We used SAS to create and manipulate the data files (30). Means were adjusted by using SUDAAN PROC DESCRIPT standardization statements and the 1980 population proportions as recommended in the NHANES III analytic guidelines (23), and we tested the geometric means for interactions between age, sex, and race-ethnicity by using SUDAAN PROC REG (29). We also obtained smoothed curves of the age-specific geometric means, by using the SYSTAT LOWESS smoothing procedure (31, 32), to reduce the difference between adjacent age categories associated with sampling variability.

The average design effect, which is the ratio of the complex sampling design variance derived from SUDAAN (29) to the simple random sample variance calculated by SAS (30), averaged over the age categories, was used to determine the recommended minimum stratum sample size according to the National Center for Health Statistics analytic guidelines and recommendations to achieve stable estimates of means and percentiles (23). On the basis of an average design effect of ≈1.4 for our sample, we identified as unstable the means for those strata in which there were <42 individuals. Individuals from other racial or ethnic groups were not considered separately in these analyses because of their small numbers (n = 436).

RESULTS

Serum total homocysteine values were measured for 8585 individuals aged ≥12 y. The sample included 1235 non-Hispanic white males, 1740 non-Hispanic white females, 1154 non-Hispanic black males, 1555 non-Hispanic black females, 1211 Mexican American males, 1254 Mexican American females, and 166 males and 270 females of other racial or ethnic origin. The distribution of participants by age group, untransformed means, and selected percentiles are provided in **Appendix A** (**Tables A1**–**A4**) for all race-ethnicity groups combined and separately for non-Hispanic whites, non-Hispanic blacks, and Mexican Americans.

The age-specific and age-adjusted geometric mean total

TABLE 1
Geometric mean serum total homocysteine concentrations by age group, sex, and race-ethnicity[1]

Age	Males			Females		
	NHW	NHB	MA	NHW	NHB	MA
	μmol/L			*μmol/L*		
12–15 y	6.8	7.4	6.8	6.1	6.5	6.0
16–19 y	8.3	8.5	9.0	6.9	7.4	6.4
20–29 y	10.1	9.4	9.1	7.4	7.5	6.9
30–39 y	9.3	9.1	9.1	7.6	7.5	6.6
40–49 y	9.4	10.0	9.0	8.0	8.0	7.2
50–59 y	10.3	11.4	10.0	8.4	9.1	8.1
60–69 y	10.5	11.5	11.2	9.6	10.2	9.3
70–79 y	11.7	12.8	11.3	10.6	10.2	9.5
≥80 y	12.4	12.4[2]	15.0[2]	11.5	13.6[2]	11.0[2]
Age adjusted[3]	9.6	9.8	9.4	7.9[4]	8.2[4]	7.4

[1] NHW, non-Hispanic whites; NHB, non-Hispanic blacks; MA, Mexican Americans.
[2] Means based on sample sizes less than those recommended to obtain stable estimates for a design effect of 1.4 ($n < 42$).
[3] Significant difference between males and females within each race-ethnicity category, $P < 0.01$.
[4] Significantly different from MA, $P < 0.01$.

homocysteine concentrations are presented in **Table 1** and the relations between geometric mean serum total homocysteine concentrations and age, sex, and race-ethnicity are displayed in **Figure 1**. The age-specific total homocysteine concentrations were lower in females than in males for each age group, except in non-Hispanic blacks aged ≥80 y. However, this latter comparison was based on only 26 non-Hispanic black men and 40 non-Hispanic black women. The age-adjusted geometric mean homocysteine concentration was significantly greater in males than in females within each race-ethnicity group ($P < 0.01$).

We found a significant age-sex interaction ($P < 0.01$), indicating that the relation between age and homocysteine concentrations differed between the sexes (Table 1 and Figure 1). Age-specific geometric mean total homocysteine concentrations tended to increase across all age categories, but the timing of the increase with age generally differed in males and females. Mean total homocysteine concentrations were modestly higher in boys than in girls aged 12–15 y. In adolescents and young adults, homocysteine concentrations increased rapidly in males across age groups; the rate of increase was more gradual in females. From age 30 to 49 y, only small differences existed in homocysteine concentrations across age groups for men and women. The rate of increase appeared to rise with age in men and women aged >50 y. The rate of increase in non-Hispanic white and non-Hispanic black females seemed to exceed that in males, resulting in a smaller difference between non-Hispanic white and non-Hispanic black males and females at older ages. For example, total homocysteine concentrations in non-Hispanic white and non-Hispanic black men aged 20–29 y were 36% and 25% greater, respectively, than in women. In the group aged ≥80 y, concentrations were 8% greater in non-Hispanic white men and 9% lower in non-Hispanic black men than in women. Mexican American females did not have a greater age-related rate of increase in homocysteine concentration than males in older age categories; the sex difference for this group was thus maintained with age.

We found differences in total homocysteine concentrations between race-ethnicity groups in females, but not in males. Mexican American females had significantly lower total homocysteine concentrations than either non-Hispanic white or non-Hispanic black females ($P < 0.01$). In each age category, geometric mean homocysteine concentrations were lowest in Mexican American females (Table 1).

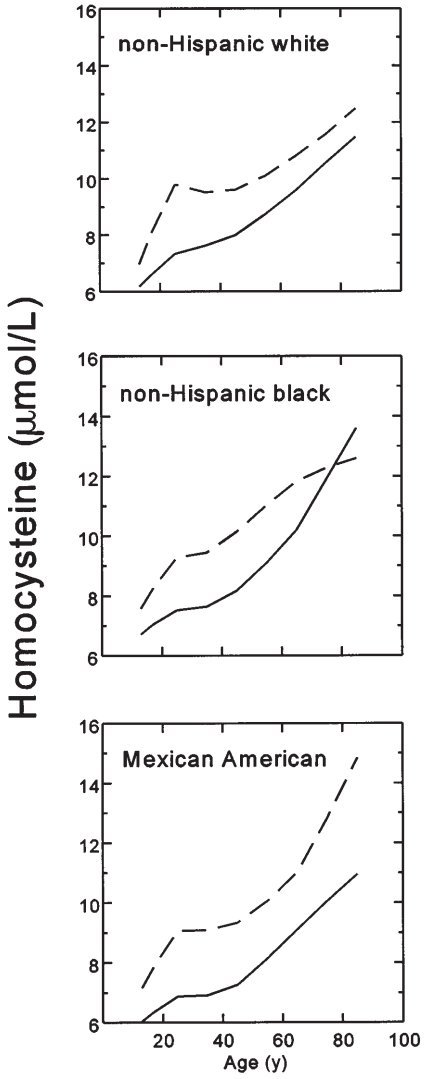

FIGURE 1. Smoothed geometric mean serum homocysteine concentration by age group, sex, and race-ethnicity in males (– – –) and females (—).

DISCUSSION

This study presents the first reference information on total homocysteine concentrations in a nationally representative sample of the US population. Our results showed that total homocysteine concentrations increased across age groups and were higher in males than in females. We also observed that Mexican American females had significantly lower total homocysteine concentrations than either non-Hispanic white or black females. This difference was evident across all age groups.

The age and sex differences are consistent with observations from other large samples of adult men and women (10, 11), but this study was the first to measure homocysteine concentrations

in a large, population-based sample of healthy adolescents and young adults. The Hordaland (Norway) Homocysteine Study (11) examined 7591 men and 8585 women aged 40- 67 y with no history of vascular disease, diabetes, or hypertension. In the youngest participants (40–42 y), total plasma homocysteine concentrations in men (10.8 μmol/L) were 19% higher than in women (9.1 μmol/L). This difference was modestly diminished to 11% in the oldest age group considered (65–67 y). Total homocysteine concentrations in these older men and women were 12.3 and 11.0 μmol/L, respectively, which was a 13% increase in men and a 21% increase in women from age 40–42 to 65–67 y. In 1160 members of the original Framingham Heart Study cohort (aged 67–96 y), total plasma homocysteine concentrations were 10% higher in men (11.8 μmol/L) than in women (10.7 μmol/L) aged <75 y, but the difference was only 4% among those aged ≥75 y (10). Total homocysteine concentrations also increased across the fairly narrow age range (67–96 y) in this elderly cohort. Men and women aged ≥80 y had total homocysteine concentrations that were ≈19% and 23% higher, respectively, than those aged <75 y.

Age- and sex-related differences in total homocysteine concentrations were also reported in smaller samples. Brattström et al (12) examined 131 men and 113 women from Sweden across a broad age range (35–95 y). They observed that men had higher total homocysteine concentrations than women at every age. In men, homocysteine concentrations steadily increased over the age groups, but concentrations in women did not appear to increase until about ≥65 y. Koehler et al (13) examined total homocysteine concentrations in a subset of 50 men and 50 women aged 68–96 y from the New Mexico Aging Process Study. Homocysteine concentrations in these elderly men averaged 15% higher than concentrations in elderly women, and concentrations increased significantly with age in these elderly subjects. Investigators measured total homocysteine concentrations in 185 Spanish children aged 2 mo to 18 y and reported that homocysteine concentrations increased significantly with age (33). Median concentrations were 5.8 μmol/L in children aged ≤10 y, 6.6 μmol/L in children aged 11–15 y, and 8.1 μmol/L in those aged 16–18 y. However, no significant differences were observed between adolescent boys and girls; the effect of puberty on homocysteine concentrations was not considered. Age was unrelated to total homocysteine concentrations in a study of 584 healthy Canadian adults (34), but this sample was fairly young (mean age: 36 y; range: 23–59 y).

The reasons for the higher homocysteine concentrations at older ages are not well understood, although changes in renal function (1) and impaired renal metabolism of homocysteine (35) are certainly involved. Higher homocysteine concentrations in males than in females may be explained by differences in body size, estrogen status, and vitamin status. There is a strong correlation between homocysteine concentrations and circulating creatinine concentrations, even in individuals with normal creatinine concentrations (12). Apart from a possible increase in creatinine at older ages that results from impaired renal function, this association may indicate increased homocysteine production as a consequence of methyl group transfer during creatine metabolism. Because creatine production is related to body size, circulating creatinine might explain part of the sex-related difference in homocysteine concentrations (12). Part of the difference in the pattern of increase in homocysteine concentrations with age in males and females could also be a consequence of an effect of estrogen on homocysteine metabolism. Our data are consistent with the possibility that there is a smaller age-related increase in homocysteine concentrations in young females after menarche and a greater age-related increase in older women after menopause. Menopause has been implicated as a determinant of total homocysteine concentrations (14, 15), but little direct evidence exists to relate estrogen concentrations to homocysteine metabolism. One uncontrolled study showed that estrogen replacement significantly lowered total homocysteine concentrations in postmenopausal women (16) and a second study showed that total homocysteine concentrations were inversely related to estradiol concentrations in premenopausal women (15). The sex differences may also be explained in part by differences in folate, vitamin B-12, and vitamin B-6 status (10).

Our study was the first to examine differences in total homocysteine concentrations between racial or ethnic groups in a large, population-based study. Few other studies considered racial or ethnic differences in circulating homocysteine concentrations. One study indicated that South African black men might have lower fasting total homocysteine concentrations than South African white men (36), but a later comparison of young South African black and white male police recruits living under similar conditions failed to show differences in total fasting homocysteine concentrations (37). After a methionine load, however, the increase in homocysteine concentration was significantly lower in the black than in the white recruits. Moreover, the increase was related to vitamin nutriture in whites, but not in blacks, suggesting metabolic differences. Another study that examined metabolic differences between US blacks and whites showed that blacks were less likely than whites to have a common defect in 5,10-methylenetetrahydrofolate reductase ($FADH_2$) (38), an enzyme that plays a central role in homocysteine metabolism. This defect results in an enzyme with reduced activity (39) and consequently higher circulating homocysteine concentrations, particularly when folate concentrations are inadequate (40). Although the NHANES III data on homocysteine concentrations cannot directly address the potential metabolic differences between whites and blacks, these data do not indicate any differences in circulating concentrations of total homocysteine between these 2 racial groups.

Our understanding of factors that influence circulating homocysteine concentrations are still incomplete. Because fairly modest elevations in total homocysteine concentration are strongly associated with a higher risk of vascular disease (1–9), it is crucial that we understand the basis for the differences that we observed: the age-related increase in total homocysteine concentrations, the influence of sex on circulating concentrations of homocysteine, and the racial and ethnic differences in females. Data such as those collected as part of NHANES III will allow these and other important questions concerning determinants of homocysteine metabolism to be addressed.

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APPENDIX A

Untransformed means and selected percentiles of serum total homocysteine concentrations by age group and sex

Untransformed mean serum homocysteine concentrations, complex-sample SDs (CSSDs), smoothed SEs (SSEs), and selected percentiles for each stratum of age, sex, and race-ethnicity are presented in **Tables A1–A4**. CSSDs and SSEs are provided because we had data from only 1 phase of a 2-phase sampling design. NHANES III was designed with 2 primary sampling units (PSUs) selected per stratum, with each assigned randomly to phase 1 or phase 2 (1). When variance estimates are computed for only one phase, strata must be collapsed, or paired, to achieve an implied 2-PSUs-per-stratum design. Although SEs from one phase can be estimated by using SUDAAN (2), they are slightly overestimated. Kish (3) discusses modeling SEs to improve the precision of the SE estimates using the design effect. Because the design effect is different for different subgroups, an average design effect is used to model, or smooth, the SE estimates. This same technique is also applied to estimates of the SD to improve the precision of those estimates. CSSDs and SSEs were calculated by using the following equations (R Forthover, unpublished observations, 1981).

$$SSE = \sqrt{\overline{DE}} \times (SD/\sqrt{n}) \qquad (A1)$$

where $\overline{DE}$ is the design effect averaged over the age categories, which is the ratio of the complex sampling design variance derived from SUDAAN (2) to the simple random sample variance calculated by SAS (4), and SD was calculated by SAS assuming a simple random sample.

$$CSSD = \sqrt{SD^2 + SSE^2} \qquad (A2)$$

where SD is the simple, random-sample SD calculated by using SAS.

On the basis of an average design effect of ≈1.4 for our sample, we identified as unstable the means and medians (50th percentiles) for those strata in which there were <42 individuals, 25th and 75th percentiles for strata in which there were <45 individuals, 15th and 85th percentiles for strata in which there were <75 individuals, and 10th and 90th percentiles for strata in which there were <112 individuals.

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TABLE A1
Untransformed means and selected percentiles of serum total homocysteine concentrations by age group and sex: combined race-ethnicity groups

Age	$\bar{x}$	Complex-sample SD	Smoothed SE	Selected percentiles						
				10th	15th	25th	50th	75th	85th	90th
	μmol/L	*μmol/L*	*μmol/L*	*μmol/L*						
Males										
12–15 y (*n* = 347)	7.4	4.4	0.37	4.5	4.9	5.5	6.7	8.0	8.9	9.3
16–19 y (*n* = 295)	8.8	3.6	0.33	5.6	5.9	6.6	8.3	9.7	11.5	11.7
20–29 y (*n* = 685)	10.5	5.6	0.34	6.5	6.8	7.6	9.3	11.3	13.0	14.4
30–39 y (*n* = 597)	9.8	5.0	0.32	6.3	6.7	7.6	8.7	10.5	11.9	13.1
40–49 y (*n* = 494)	10.0	3.9	0.28	6.3	6.8	7.6	8.9	11.3	13.1	14.5
50–59 y (*n* = 311)	12.3	11.5	1.03	7.3	7.7	8.3	10.1	12.7	14.2	15.3
60–69 y (*n* = 499)	11.5	7.6	0.54	7.2	7.6	8.5	10.4	12.8	13.8	15.2
70–79 y (*n* = 298)	13.0	8.0	0.73	7.8	8.3	9.2	11.6	15.4	17.1	18.1
≥80 y (*n* = 240)	13.6	6.3	0.64	7.8	8.6	9.4	12.2	16.1	19.1	20.5
Females										
12–15 y (*n* = 415)	6.5	2.8	0.23	3.8	4.2	4.9	6.0	7.4	8.2	8.6
16–19 y (*n* = 345)	7.2	2.7	0.25	4.2	4.9	5.6	6.7	8.1	9.2	10.0
20–29 y (*n* = 865)	7.9	3.5	0.20	4.8	5.1	5.7	7.0	9.1	10.7	12.0
30–39 y (*n* = 891)	7.9	3.4	0.20	5.0	5.3	5.9	7.2	8.9	10.4	11.5
40–49 y (*n* = 628)	8.6	5.0	0.34	4.9	5.5	6.1	7.5	9.4	11.1	12.7
50–59 y (*n* = 469)	9.0	4.0	0.32	5.4	6.0	6.7	8.4	10.2	11.8	13.1
60–69 y (*n* = 475)	10.3	4.0	0.31	6.3	7.1	7.8	9.5	11.5	13.3	14.7
70–79 y (*n* = 448)	11.4	6.5	0.53	6.8	7.3	8.2	10.3	13.3	14.9	16.3
≥80 y (*n* = 283)	12.6	6.3	0.64	7.3	7.7	8.8	11.3	14.1	16.6	19.0

TABLE A2
Untransformed means and selected percentiles of serum total homocysteine concentrations by age group and sex: non-Hispanic whites

Age	$\bar{x}$	Complex-sample SD	Smoothed SE	Selected percentiles						
				10th	15th	25th	50th	75th	85th	90th
	μmol/L	μmol/L	μmol/L	μmol/L						
Males										
12–15 y (n = 68)	7.4	4.4	0.56	4.3[1]	4.9[1]	5.5	6.6	7.9	8.7[1]	9.2[1]
16–19 y (n = 50)	8.7	2.8	0.41	5.4[1]	5.9[1]	6.2	8.3	10.5	11.5[1]	11.7[1]
20–29 y (n = 158)	11.0	6.3	0.52	6.5	7.0	8.0	9.6	11.7	13.5	15.1
30–39 y (n = 141)	9.9	5.1	0.45	6.5	6.9	7.7	8.9	10.6	12.4	13.2
40–49 y (n = 148)	9.9	3.6	0.31	6.3	6.7	7.6	8.9	11.3	12.8	14.4
50–59 y (n = 131)	10.9	3.7	0.34	7.1	7.6	8.2	10.1	12.7	13.8	14.8
60–69 y (n = 206)	11.5	8.3	0.60	6.9	7.5	8.4	10.4	12.4	13.7	15.2
70–79 y (n = 158)	12.8	8.3	0.69	7.7	8.2	9.2	11.2	14.8	16.4	17.6
≥80 y (n = 175)	13.4	6.0	0.47	7.7	8.8	9.5	12.2	16.1	18.9	20.0
Females										
12–15 y (n = 88)	6.5	2.9	0.38	3.6[1]	4.1	4.9	5.9	7.3	7.8	8.2[1]
16–19 y (n = 61)	7.5	3.1	0.49	3.9[1]	4.9[1]	5.6	6.9	8.7	9.7[1]	10.2[1]
20–29 y (n = 216)	8.0	3.6	0.30	4.8	5.1	5.7	7.1	9.4	11.0	12.1
30–39 y (n = 257)	8.1	3.6	0.28	5.1	5.4	6.1	7.3	8.9	10.6	11.9
40–49 y (n = 200)	8.8	5.1	0.45	4.9	5.5	6.2	7.7	9.6	11.5	13.1
50–59 y (n = 218)	8.9	3.4	0.29	5.4	5.8	6.7	8.3	9.9	11.6	13.0
60–69 y (n = 191)	10.2	3.8	0.34	6.4	7.1	7.8	9.5	11.4	13.0	14.5
70–79 y (n = 305)	11.5	6.8	0.49	6.8	7.3	8.2	10.3	13.4	15.0	16.5
≥80 y (n = 204)	12.4	6.3	0.54	7.4	7.8	8.7	11.1	14.0	16.4	18.2

[1] Values based on sample sizes that did not meet the recommended number needed to obtain stable estimates for a design effect of 1.4: n < 42 for means, 50th percentiles, SDs, and SEs; n < 75 for the 15th and 85th percentiles; and n < 112 for the 10th and 90th percentiles.

TABLE A3
Untransformed means and selected percentiles of serum total homocysteine concentrations by age group and sex: non-Hispanic blacks

Age	$\bar{x}$	Complex-sample SD	Smoothed SE	Selected percentiles						
				10th	15th	25th	50th	75th	85th	90th
	μmol/L	μmol/L	μmol/L	μmol/L						
Males										
12–15 y (n = 141)	7.9	3.1	0.29	4.9	5.2	5.9	7.1	8.8	10.2	11.2
16–19 y (n = 125)	9.3	6.0	0.58	5.4	6.0	6.5	8.3	9.6	10.7	12.4
20–29 y (n = 213)	9.8	3.2	0.24	6.6	7.1	7.9	9.1	11.1	12.2	13.1
30–39 y (n = 225)	9.7	5.0	0.36	6.4	6.7	7.5	8.7	10.2	11.7	13.1
40–49 y (n = 151)	10.8	5.8	0.52	6.8	7.2	8.0	9.5	11.9	14.2	15.2
50–59 y (n = 87)	12.3	6.2	0.72	7.7[1]	8.3	9.0	10.8	13.3	15.2	17.4[1]
60–69 y (n = 120)	12.3	5.2	0.52	7.4	7.8	8.9	11.9	14.0	15.4	17.1
70–79 y (n = 66)	13.8	5.7	0.76	7.9[1]	8.5[1]	9.0	13.0	17.1	18.8[1]	20.2[1]
≥80 (n = 26)	13.4[1]	5.8[1]	1.21[1]	8.2[1]	8.3[1]	9.3[1]	11.6[1]	15.0[1]	17.7[1]	19.9[1]
Females										
12–15 y (n = 175)	6.8	2.6	0.23	4.4	4.7	5.3	6.1	7.7	9.0	9.7
16–19 y (n = 151)	7.8	2.6	0.25	5.2	5.6	6.2	7.1	8.7	10.0	11.4
20–29 y (n = 310)	8.0	3.0	0.21	4.9	5.3	6.0	7.3	9.2	10.5	11.5
30–39 y (n = 337)	8.0	3.2	0.21	4.9	5.5	6.0	7.1	9.1	10.5	11.4
40–49 y (n = 244)	8.7	5.0	0.38	5.6	5.8	6.2	7.6	9.6	10.9	12.0
50–59 y (n = 127)	10.0	7.6	0.82	5.7	6.0	7.1	9.0	10.9	12.0	14.5
60–69 y (n = 111)	11.0	4.9	0.56	6.2[1]	6.7	7.7	9.7	13.3	14.2	15.3[1]
70–79 y (n = 60)	11.0	4.9	0.76	6.4[1]	7.0[1]	7.8	9.6	12.9	14.1[1]	15.6[1]
≥80 y (n = 40)	14.9[1]	6.9[1]	1.31[1]	7.7[1]	9.7[1]	10.3[1]	12.9[1]	16.4[1]	19.5[1]	21.6[1]

[1] Values based on sample sizes that did not meet the recommended number needed to obtain stable estimates for a design effect of 1.4: n < 42 for means, 50th percentiles, SDs, and SEs; n < 45 for the 25th and 75th percentiles; n < 75 for the 15th and 85th percentiles; and n < 112 for the 10th and 90th percentiles.

TABLE A4
Untransformed means and selected percentiles of serum total homocysteine concentrations by age group and sex: Mexican Americans

Age	$\bar{x}$	Complex-sample SD	Smoothed SE	Selected percentiles						
				10th	15th	25th	50th	75th	85th	90th
	μmol/L	*μmol/L*	*μmol/L*	*μmol/L*						
Males										
12–15 y (*n* = 118)	7.8	7.0	0.84	4.4	4.7	5.2	6.5	7.8	9.4	10.0
16–19 y (*n* = 106)	9.6	3 9	0.50	6.1[1]	6.5	7.1	8.8	11.4	12.9	13.8[1]
20–29 y (*n* = 281)	9.6	4.1	0.32	6.3	6.7	7.4	8.8	10.5	11.9	13.3
30–39 y (*n* = 203)	9.8	5.8	0.53	6.2	6.6	7.1	8.7	10.6	12.1	13.3
40–49 y (*n* = 179)	9.4	3.0	0.29	6.1	6.7	7.6	9.0	10.6	11.6	12.3
50–59 y (*n* = 76)	10.9	6.6	0 99	7.2[1]	7.6	8.2	9.6	11.5	13.0	13.5[1]
60–69 y (*n* = 154)	11.7	3.8	0.40	7.4	8.0	9.3	10.8	13.5	14.6	15.0
70–79 y (*n* = 65)	12.0	5.0	0.80	8.0[1]	8.6[1]	9.3	10.6	13.4	14.8[1]	15.8[1]
≥80 (*n* = 29)	17.7[1]	12.7[1]	3.01[1]	8.5[1]	8.7[1]	9.4[1]	13.1[1]	19.9[1]	24.1[1]	27.1[1]
Females										
12–15 y (*n* = 125)	6.5	3.7	0.37	4.2	4.4	4.7	5.9	7.1	8.1	8.5
16–19 y (*n* = 109)	6.6	1.8	0.20	4.2[1]	4.8	5.4	6.3	7.7	8.5	9.0[1]
20–29 y (*n* = 295)	7.5	3.6	0.24	4.5	4.7	5.5	6.7	8.5	9.9	10.4
30–39 y (*n* = 251)	7.0	2.7	0.19	4.3	4.7	5.3	6.4	7.9	8.8	9.7
40–49 y (*n* = 156)	7.8	4.4	0.40	4.8	5.1	5.7	6.8	8.7	9.9	10.6
50–59 y (*n* = 84)	8.3	1.9	0.24	5.9[1]	6.2	6.8	7.9	9.2	10.4	11.3[1]
60–69 y (*n* = 144)	9.8	3.6	0.34	6.1	6.7	7.4	9.0	11.1	12.8	13.6
70–79 y (*n* = 61)	9.9	3.5	0.50	6.2[1]	6.3[1]	7.3	9.6	10.7	12.5[1]	13.3[1]
≥80 y (*n* = 29)	11.6[1]	4.0[1]	0.83[1]	—[2]	6.5[1]	8.7[1]	11.2[1]	15.1[1]	15.6[1]	15.9[1]

[1] Values based on sample sizes that did not meet the recommended number needed to obtain stable estimates for a design effect of 1.4: $n < 42$ for means, 50th percentiles, SDs, and SEs; $n < 45$ for the 25th and 75th percentiles; $n < 75$ for the 15th and 85th percentiles; and $n < 112$ for the 10th and 90th percentiles.

[2] SUDAAN (2) was unable to extrapolate to compute the 10th percentile.