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Serum Androgen Levels in Black, Hispanic, and White Men

Heather J. Litman, Shalender Bhasin, Carol L. Link, Andre B. Araujo, and John B. McKinlay, for the Boston Area Community Health Survey Investigators

New England Research Institutes (H.J.L., C.L.L., A.B.A., J.B.M.), Watertown, Massachusetts 02472; and Section of Endocrinology, Diabetes, and Nutrition (S.B.), Boston University, School of Medicine, Boston Medical Center, Boston Massachusetts 02118

Context: Racial/ethnic differences in androgen levels could account for differences in prostate cancer risk, body composition, and bone loss.

Objective: The objective of the study was to investigate racial/ethnic variations in testosterone, bioavailable testosterone, dihydrotestosterone (DHT), SHBG, and dehydroepiandrosterone sulfate (DHEAS) levels.

Design: The Boston Area Community Health (BACH) Survey was a multistage stratified cluster random sample, recruiting from 2002 to 2005.

Setting: The study was a community-based sample of Boston.

Participants: Participants included black, Hispanic, or white individuals, aged 30–79 yr, competent to sign informed consent and literate in English/Spanish. Of 2301 men recruited, 1899 provided blood samples (538 black, 651 Hispanic, 710 white).

Intervention: Intervention consisted of data obtained during in-person at-home interview, conducted by a bilingual phlebotomist/interviewer.

Main Outcome Measure(s): Testosterone, bioavailable testosterone, DHT, DHT to testosterone ratio, SHBG, and DHEAS were measured.

Results: With or without adjustment for covariates, there were no significant differences in testosterone, bioavailable testosterone, or SHBG levels by race/ethnicity. DHEAS levels differed by race/ethnicity before covariate adjustment; after adjustment this difference was attenuated. Before adjustment, DHT and DHT to testosterone ratios did not significantly differ by racial/ethnic group. After adjustment, there was evidence of racial/ethnic differences in DHT ($P = 0.047$) and DHT to testosterone ($P = 0.038$) levels. Black men had higher DHT levels and DHT to testosterone ratios than white and Hispanic men.

Conclusions: Because there are no racial/ethnic differences in testosterone levels, normative ranges need not be adjusted by race/ethnicity for androgen deficiency diagnosis for men aged 30–79 yr. Further investigation is needed to determine whether differences in DHT levels and DHT to testosterone ratio can help explain racial/ethnic variations in prostate cancer incidence, body composition, and bone mass. **(*J Clin Endocrinol Metab* 91: 4326–4334, 2006)**

ALTHOUGH RACIAL/ETHNIC differences in circulating total testosterone levels have been examined previously (1–9), the results of the published studies are not in agreement. Some studies reported higher unadjusted testosterone levels among blacks than whites (3, 4, 8, 9); others found no differences in circulating (1, 2, 6, 7) or tissue (5) total testosterone concentrations. Some studies (1, 2, 5, 6) reported no racial/ethnic differences in 5α-dihydrotestosterone (DHT), and one study (9) found statistically significantly higher DHT levels in blacks, compared with whites. Most studies included relatively older men (average age > 50 yr). A study of young men reported higher unadjusted total testosterone levels in blacks, compared with whites (4); however, after adjusting for waist circumference, there were no significant racial/ethnic differences. Most studies (1, 2, 5–8), with some exceptions (3, 4), included small numbers of blacks, and none had significant representation of Hispanics.

Racial/ethnic differences in androgen levels could have clinical implications for the diagnosis of androgen deficiency syndromes and explaining racial/ethnic differences in the prevalence of clinical prostate cancer, body composition, and bone loss in men. We do not know whether normative ranges for testosterone levels, crucial for making the diagnosis of androgen deficiency in men, should be adjusted for race/ethnicity. Androgens, particularly testosterone and DHT (10, 11), regulate prostate epithelial growth and promote growth of metastatic prostate cancer. Prostate cancer is the most prevalent cancer among men living in the United States (12) and a significant contributor to morbidity and mortality in older men (13, 14). Even after adjustment for age, the incidence rate of prostate cancer among blacks is 1.5 times higher than among whites and more than two times higher than among Hispanics (6, 14). Differences in testosterone and/or DHT levels have been hypothesized to explain racial/ethnic differences in androgen-related disorders (15, 16). Androgens are also important determinants of body composition and skeletal mass; racial/ethnic differences in androgen lev-

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Abbreviations: BACH, Boston Area Community Health; BMI, body mass index; CV, coefficient of variation; DHEAS, dehydroepiandrosterone sulfate; DHT, 5α-dihydrotestosterone; MCS12, mental health component score; PASE, Physical Activity Scale for the Elderly; PCS12, physical health component score; SES, socioeconomic status; SRD5A2, steroid 5α-reductase type II; WHR, waist to hip ratio.

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els may help explain the observed differences in body composition (17) including higher muscle mass and strength (18), bone mineral density (19), and lower rates of age-related bone loss (20) and fracture incidence (18, 21–35) in blacks, compared with other racial/ethnic groups.

The Boston Area Community Health (BACH) Survey of community-dwelling adult men allowed us to investigate racial/ethnic variations in testosterone and dehydroepiandrosterone sulfate (DHEAS) levels, the two most abundant androgens in circulation, and DHT, a metabolite of testosterone that is formed by the action of steroid 5α-reductase. Because differences in body composition, particularly body mass index, could affect SHBG levels and thereby influence total testosterone levels, we also measured SHBG levels (10). Bioavailable testosterone levels were calculated; they provide an SHBG-independent measure of circulating testosterone. The ratio of DHT to testosterone was also investigated because it provides an indirect measure of steroid 5α-reductase activity (9).

In contrast to previous studies, the BACH Survey included men over a wide age range (13) with approximately equal numbers of blacks, whites, and Hispanics, the three major racial/ethnic groups in the United States. Because circulating androgen concentrations are affected significantly by anthropometric measures, age, and comorbid conditions, we included these covariates in the analyses.

Subjects and Methods

The protocols and informed consent procedures were approved by the New England Research Institutes Institutional Review Board. All participants provided written, informed consent.

Overall design

The BACH Survey is a population-based epidemiological survey of a broad range of urological symptoms among randomly chosen people. Individuals from selected census blocks were chosen to achieve the goal of approximately equal numbers of black, white, and Hispanic men and women in four age categories: 30–39, 40–49, 50–59, and 60–79 yr. Sampling proceeded in five batches, each a random subsample of the overall BACH Survey. Eligibility rules varied by batch and were randomly assigned to selected households based on household demographics at the start of each batch. BACH eligibility criteria included: screened eligible from selected household, competent to sign informed consent, and able to speak English or Spanish well enough to complete the survey. The BACH sample (n = 5506) was recruited from April 2002 through June 2005; this manuscript considers men only. Because of design requirements, the BACH subjects had unequal probabilities of selection into the study. To be representative of the city of Boston, observations were weighted inversely proportional to their probability of selection into the study (36).

Data collection

Data were obtained during a 2-h interview, conducted by a bilingual phlebotomist/interviewer, generally in the subject's home (37). After written informed consent, a venous blood sample (20 ml) and height, weight, hip and waist circumference were measured along with self-reported information on medical and reproductive history, major comorbidities, prescription and over-the-counter medications, lifestyles, psychosocial factors, medical care use, and symptoms of urogynecological conditions. Blood samples were collected close to waking time (median time since awakening 3 h 38 min).

Race/ethnicity

Race/ethnicity involved a two-step self identification process. Each subject was first asked: do you consider yourself to be Spanish, Hispanic, or Latino? If the respondents answered yes, they were asked to specify their Hispanic origin. Subjects were then asked: what race do you consider yourself to be, with the option of choosing any or all of the following categories: American Indian/Alaska Native, Asian, black/African-American, Native Hawaiian/other Pacific Islander, white/Caucasian, or other. Men were categorized as Hispanic if they responded yes to the Hispanic question. Non-Hispanic respondents were categorized as black if they stated they were black/African American, regardless of whether they checked more than one race. Men were classified as white if they stated they were white/Caucasian, provided they were not already classified as Hispanic or black.

Hormones

Testosterone, SHBG, and DHEAS levels were measured by competitive electrochemiluminescence immunoassays on the 2010 Elecsys system (Roche Diagnostics, Indianapolis, IN); DHT was measured by a RIA (Diagnostic Systems Laboratories, Webster, TX). All assays were approved previously by the Food and Drug Administration for clinical use. The lower limits of detection for testosterone, DHT, SHBG, and DHEAS assays were 2 ng/dl (0.07 nmol/liter), 0.4 ng/dl (0.014 nmol/liter), 3 nmol/liter, and 0.001 μg/ml (0.0027 μmol/liter), respectively. The interassay coefficients of variation (CVs) for testosterone at concentrations of 24 (0.83), 275 (9.54), and 701 (24.31) ng/dl (nmol/liter) were 7.4, 2.2, and 1.7%, respectively; intraassay CVs were 4.6, 1.4, and 1.1% at the same concentrations. The interassay CVs for DHT at concentrations 10.6 (0.37), 31.1 (1.08), and 71.1 (2.47) ng/dl (nmol/liter) were 8.5, 2.3, and 8.4%, respectively; intraassay CVs were 6.2, 4.5, and 3.1% at concentrations 9.7 (0.34), 29.0 (1.00), and 68.5 (2.38) ng/dl (nmol/liter). The cross-reactivity of testosterone and DHEA in the DHT assay were 0.02% and nondetectable, respectively. To establish accuracy, known amounts of DHT, ranging from 23 to 85 ng/dl were added to charcoal-stripped plasma; the recovery ranged from 90 to 117% (mean 105%). At 25, 64, and 95 nmol/liter, interassay CVs were 2.4, 2.2, and 2.7%; at 14, 44, and 204 nmol/liter, intraassay CVs were 2.1, 2.4, and 2.7% for SHBG. For DHEAS, at 117 (3.18), 395 (10.72), and 984 (26.71) μg/dl (μmol/liter), interassay CVs were 3.6, 4.7, and 2.4%; at the same concentrations, intraassay CVs were 2.8, 2.4, and 1.7%.

Bioavailable testosterone was calculated from total testosterone and SHBG concentrations using published equations (38), assuming an albumin concentration of 4.3 g/dl and association constants of SHBG for testosterone 1.0×10^9/mol and albumin for testosterone 3.6×10^4/mol (39). Calculated free testosterone was not considered because it is a linear function of calculated bioavailable testosterone; thus, linear models on free testosterone will produce identical results to those on bioavailable testosterone.

Covariates

Categorical covariates included body mass index (BMI) defined as measured weight in kilograms divided by measured height in squared meters categorized as less than 25 (reference), 25–29, 30 + kg/m^2; waist to hip ratio (WHR) calculated as the ratio of waist to hip measurements, divided into quartiles; smoking status: current, previous, never (reference); alcohol (including beer, wine, and hard liquor) consumed per day [none (reference), less than 1, 1–2, 3 or more drinks per day]; comorbidities including diabetes, cancer, heart conditions, high cholesterol, high blood pressure, vascular conditions, prior urinary tract infections, asthma, and arthritis; and depressive symptoms based on reporting five or more symptoms on the abbreviated Center for Epidemiologic Studies-Depression scale (40).

Continuous covariates included age (years), physical activity as measured by the Physical Activity Scale for the Elderly (PASE) (41) and the physical and mental health component scores [physical health component score (PCS12), mental health component score (MCS12)] based on the Medical Outcome 12-Item Short-Form Health Survey SF-12 quality-of-life assessment (42). The SF-12 consisted of questions regarding physical and mental health; the PCS12 was constructed by weighting physical health questions higher and conversely for the MCS12 scale. Also considered was socioeconomic status (SES), created as a function of standardized income and education variables for the northeast region (43). Because of the diurnal variation in hormone values, analyses controlled for the number of hours between waking and subjects' blood draws.

Statistical analysis

Hormone variables were log-base 10 transformed because their distributions were skewed. The median and the interquartile range were calculated; means are also presented. Seven men with low testosterone [<20 ng/dl (0.69 nmol/liter] and low DHT [<6.0 ng/dl (0.21 nmol/liter] values were excluded from the analyses; all reported having cancer [prostate cancer (four), testicular cancer (one), colon cancer and prostate surgery (one), skin cancer (one)]. Another man with a testosterone value of 3710 ng/dl (128.64 nmol/liter) and an undetectable LH value as well as two men with DHT values greater than 500 ng/dl (17.34 nmol/liter) were also excluded. Results were similar with and without the 10 extreme values (not presented). Weighted analyses were conducted in SAS/SUDAAN (44) and plots on the log scale were created using S-PLUS (45). A multiple imputation technique was used to impute missing covariate values (46). The largest amount of missingness was in reporting SES, which was missing for 102 (5%) of the 1899 men.

The testosterone, bioavailable testosterone, DHT, DHT to testosterone ratio, SHBG, and DHEAS values were treated as dependent variables and modeled adjusting for age using multivariate linear regression. Because observations in the BACH Survey must be weighted inversely proportional to the probability of selection, a standard forward selection procedure (as in SAS) was not available. The following manual forward selection procedure was followed using SUDAAN. First, the relationship between each covariate and the hormone considered was found (see Tables 2 and 3). Variables with individual P values less than 0.5 were considered as possible covariates for the final model. In order of significance level based on Wald F tests for each covariate (smallest P value first), models with an increasing number of covariates were fit until only covariates with Wald F test ($P < 0.05$) adjusting for the other variables were kept; this was deemed the parsimonious model. Age and hours blood taken from awakening were left in all multivariate models regardless of significance level. This technique does not account for multiple comparisons. Residual plots were constructed to check appropriate model fit; in addition, continuous covariates were considered as categorical ones with varying categories to assess the sensitivity of test statistics.

Results

In total, 5506 people (2301 men, 3205 women) aged 30–79 yr were recruited to the BACH Survey. We consider only men; 1899 provided blood samples, including 538 blacks (28%), 651 Hispanics (34%), and 710 whites (38%). The distribution of age was nearly equivalent with 511 (27%) aged 30–39 yr (127 black, 209 Hispanic, 175 white), 555 (29%) aged 40–49 yr (174 black, 195 Hispanic, 186 white), 437 (23%) aged 50–59 yr (130 black, 139 Hispanic, 168 white) and 396 (21%) aged 60–79 yr (107 black, 108 Hispanic, 181 white). Testosterone, SHBG, and DHEAS levels were obtained for 1892 participants; DHT levels were obtained for 1891. One testosterone, three DHT, and two SHBG and DHEAS values were not calculated due to insufficient serum quantity. After also deleting the 10 aforementioned outliers, analyses for testosterone involved 1881, DHT 1878, and SHBG and DHEAS 1880 participants.

The distributions of covariates such as age, PCS12, SES, WHR, smoking status and drinks per day differed significantly by racial/ethnic group (Table 1). Serum total testosterone levels were highly correlated with SHBG, bioavailable testosterone, and DHT levels (Table 2). Bioavailable testosterone levels were not correlated significantly with SHBG, consistent with the notion that bioavailable testosterone provides an SHBG-independent measure of circulating testosterone. These correlations remained similar when considered by racial/ethnic group (data not presented). Correlations between continuous covariates and hormone levels are presented in Table 2 and univariate relationships between categorical covariates and hormone levels in Table 3.

TABLE 1. Distributions of covariates potentially related to androgen levels from the BACH Survey overall and by racial/ethnic group: mean (SE) for continuous variables and percent in each category for categorical variables

Variable	Black	Hispanic	White	Total	P value[a]
n	538	651	710	1899	
Age (yr)	47.67 (0.75)	44.24 (0.53)	48.19 (0.70)	47.45 (0.48)	<0.001
PASE	197.52 (6.50)	189.43 (7.12)	181.17 (6.45)	186.34 (4.46)	0.182
PCS12	48.93 (0.55)	50.75 (0.43)	50.89 (0.51)	50.38 (0.34)	0.017
MCS12	49.66 (0.67)	51.38 (0.49)	50.34 (0.56)	50.31 (0.40)	0.066
SES	53.30 (0.54)	48.97 (0.78)	61.77 (0.53)	57.98 (0.42)	<0.001
Hours blood taken from awakening	4.41 (0.19)	4.74 (0.18)	4.43 (0.15)	4.47 (0.11)	0.369
BMI (kg/m^2)	29.25 (0.36)	28.53 (0.29)	28.43 (0.42)	28.65 (0.28)	0.121
<25	26.8	26.3	26.8	26.8	
25–29	33.4	41.3	41.7	39.5	
30+	39.9	32.4	31.4	33.7	
WHR	0.90 (0.004)	0.92 (0.005)	0.93 (0.005)	0.92 (0.003)	0.005
First quartile	31.2	23.6	22.0	24.5	
Second quartile	29.3	26.4	23.6	25.4	
Third quartile	19.4	24.3	27.8	25.3	
Fourth quartile	20.1	25.8	26.5	24.8	
Smoking status					0.003
Current	32.8	25.0	22.8	25.6	
Previous	22.4	23.5	32.6	28.8	
Never	44.9	51.5	44.6	45.6	
Alcoholic drinks per day					<0.001
None	33.8	33.3	21.6	26.2	
<1	35.0	40.0	42.4	40.2	
1–2	18.8	17.5	28.1	24.4	
3+	12.3	9.3	7.9	9.2	

[a] For continuous variables P values are from F tests comparing means of the racial/ethnic groups and for categorical variables P values are from χ^2 tests of independence between the racial/ethnic groups. All means and percents presented in the table are weighted inversely to the probability of selection.

TABLE 2. Bivariate associations and corresponding *P* values[a] for the relationships between androgens [testosterone (T), bioavailable testosterone (BT), DHT, DHT to testosterone (DHT:T) ratio, SHBG, DHEAS] on the log scale and continuous covariates from the BACH Survey (2002–2005)

	T	BT	DHT	DHT:T	SHBG	DHEAS
T	1.0					
BT	0.84 (<0.001)	1.0				
DHT	0.62 (<0.001)	0.43 (<0.001)	1.0			
DHT:T	−0.19 (<0.001)	−0.27 (<0.001)	0.66 (<0.001)	1.0		
SHBG	0.49 (<0.001)	−0.06 (0.168)	0.44 (<0.001)	0.08 (0.075)	1.0	
DHEAS	0.17 (<0.001)	0.41 (<0.001)	0.08 (0.022)	−0.06 (0.084)	−0.34 (<0.001)	1.0
Age (yr)	−0.10 (0.017)	−0.37 (<0.001)	−0.01 (0.685)	0.08 (0.071)	0.41 (<0.001)	−0.58 (<0.001)
PASE	0.11 (0.004)	0.18 (<0.001)	−0.02 (0.642)	−0.13 (0.002)	−0.07 (0.097)	0.20 (<0.001)
PCS12	0.17 (<0.001)	0.29 (<0.001)	0.02 (0.597)	−0.14 (0.004)	−0.13 (0.002)	0.27 (<0.001)
MCS12	0.03 (0.422)	0.04 (0.411)	−0.05 (0.216)	−0.09 (0.028)	0.01 (0.843)	0.01 (0.746)
SES	0.09 (0.003)	0.12 (<0.001)	0.00 (0.894)	−0.08 (0.026)	−0.02 (0.640)	0.14 (<0.001)
Hours blood taken from awakening	−0.19 (<0.001)	−0.21 (<0.001)	−0.11 (0.003)	0.04 (0.264)	−0.01 (0.680)	−0.05 (0.193)

[a] *P* values calculated incorporating weights inversely proportional to the probability of selection into the study.

Unadjusted testosterone values did not vary by racial/ethnic group (Table 4); testosterone values across age also did not vary by racial/ethnic group (Fig. 1A). These findings were confirmed by a linear regression analysis where the *P* value for the racial/ethnic difference was 0.942 after adjusting for age. The most parsimonious model to describe testosterone levels included age, BMI, WHR, smoking status, PCS12, and hours blood taken from awakening. After covariate adjustment, BMI and WHR had inverse relationships with testosterone levels, whereas smoking and PCS12 were positively related to testosterone. In the adjusted model, no significant difference in testosterone levels by race/ethnicity was found ($P = 0.900$).

Bioavailable testosterone levels did not differ significantly across racial/ethnic groups in unadjusted analysis (Table 4) or across age (Fig. 1B); the linear regression model accounting only for age ($P = 0.992$) confirms this. In a multivariate model to describe bioavailable testosterone levels including age, BMI, PCS12, smoking status, SES, and hours blood taken from awakening, bioavailable testosterone levels did not differ by race/ethnicity ($P = 0.543$). Controlling for other variables, age and BMI were associated with lower bioavailable testosterone levels, whereas PCS12, smoking status, and higher SES were associated with higher bioavailable testosterone levels.

Although unadjusted analysis (Table 4) and a linear regression model adjusting for age did not find differences in DHT levels by racial/ethnic group ($P = 0.119$) (Fig. 1C), after adjusting additionally for BMI and hours blood taken from awakening (Table 5), the racial/ethnic differences were statistically significant ($P = 0.047$). Blacks had significantly higher DHT levels, compared with Hispanics ($P = 0.034$) and whites ($P = 0.031$); DHT levels for Hispanics and whites did not differ ($P = 0.829$). Based on the multivariate model, the mean DHT level of a 40-yr-old black whose blood was drawn 2 h from awakening with BMI less than 25 kg/m^2 would be approximately 51.2 ng/dl (1.78 nmol/liter), whereas the level for a white would be 46.7 ng/dl (1.62 nmol/liter) and a Hispanic 46.2 ng/dl (1.60 nmol/liter). Yusuf *et al.* (47) have suggested WHR rather than BMI as a better measure of adiposity (regarding myocardial infarction risk). The race/ethnicity coefficients comparing models with BMI and/or WHR are presented in Table 6. When considering both BMI and WHR as covariates, BMI was found to be more predictive of DHT levels.

In unadjusted analysis, a marginal racial/ethnic difference in DHT to testosterone ratio was found (Table 4 where $P = 0.051$), and a small difference in the ratio by race/ethnicity was seen (Fig. 1D). Adjusting only for age, there was marginal evidence of a relationship between racial/ethnic group

TABLE 3. Categorical covariates as univariate predictors[a] of hormone levels [testosterone (T), bioavailable testosterone (BT), DHT, DHT to testosterone (DHT:T) ratio, SHBG, DHEAS] on the log scale from the BACH Survey (2002–2005)

	T	BT	DHT	DHT:T	SHBG	DHEAS
Race/ethnicity	0.955	0.313	0.121	0.051	0.128	0.027
BMI	<0.001	<0.001	<0.001	0.730	<0.001	0.006
WHR	<0.001	<0.001	<0.001	0.363	0.014	<0.001
Smoking status	<0.001	<0.001	0.052	0.221	<0.001	<0.001
Alcoholic drinks per day	0.002	<0.001	0.009	0.991	0.062	<0.001
Diabetes	0.002	<0.001	0.302	0.232	0.041	<0.001
Cancer	0.198	<0.001	0.734	0.131	<0.001	<0.001
Heart disease	0.003	<0.001	0.223	0.194	0.013	<0.001
High cholesterol	<0.001	<0.001	0.010	0.971	0.173	<0.001
High blood pressure	0.003	<0.001	0.048	0.725	<0.001	<0.001
Vascular conditions	0.419	0.058	0.920	0.561	0.061	0.001
Urinary tract infections	0.719	0.380	0.358	0.085	0.611	0.104
Asthma	0.898	1.000	0.900	0.753	0.604	0.843
Arthritis	0.028	<0.001	0.584	0.097	<0.001	<0.001
Depressive symptoms	0.602	0.214	0.122	0.089	0.426	0.201

[a] *P* values are from Wald F tests for the overall effect of each covariate for modeling hormone levels calculated incorporating weights inversely proportional to the probability of selection into the study.

TABLE 4. Unadjusted[a] summary statistics (mean, median, interquartile range[b]) for androgen levels (testosterone, bioavailable testosterone, DHT, SHBG, and DHEAS) among men providing blood samples (n = 1899[c]) in the BACH Survey (2002–2005) and by racial/ethnic group (black, Hispanic, white)

	Black	Hispanic	White	Total	*P* value[d]
Testosterone (ng/dl)[e]					
n	531	648	702	1881	
Mean	454	441	434	440	0.956
Median (IQR)	425 (274)	404 (219)	418 (249)	418 (253)	
Bioavailable testosterone (ng/dl)[e]					
n	531	648	701	1880	
Mean	217	223	210	213	0.313
Median (IQR)	206 (116)	214 (117)	196 (104)	201 (109)	
DHT (ng/dl)[e]					
n	529	648	701	1878	
Mean	47.8	43.6	44.4	45.2	0.121
Median (IQR)	36.9 (25.4)	35.3 (20.0)	35.1 (19.7)	35.4 (20.9)	
DHT to testosterone (DHT:T) ratio[e]					
n	528	648	701	1877	
Mean	0.1083	0.0996	0.1045	0.1048	0.051
Median (IQR)	0.0969 (0.0580)	0.0881 (0.0494)	0.0877 (0.0520)	0.0903 (0.0529)	
SHBG (nmol/liter)					
n	531	648	701	1880	
Mean	36.0	32.0	34.2	34.3	0.128
Median (IQR)	30.6 (20.2)	27.5 (17.9)	30.3 (19.5)	30.3 (19.2)	
DHEAS (μg/ml)[f]					
n	531	648	701	1880	
Mean	1.93	2.10	2.04	2.02	0.027
Median (IQR)	1.80 (1.67)	1.97 (1.38)	1.90 (1.44)	1.88 (1.50)	

[a] Summary statistics were not adjusted for the effects of age or other covariates, but because of the design of the BACH Survey, summary statistics were based on observations weighted unequally according to probabilities of selection into the study.

[b] Interquartile range (IQR) was calculated as the difference of the 25th and 75th percentiles and provides a robust measure of variation for skewed data, such as hormone values.

[c] Of the 1899 men providing blood samples, seven did not have hormone values; in addition, one did not have a DHT value. One testosterone, three DHT, two SHBG, and two DHEAS values were not calculated due to insufficient quantity. Ten subjects with extreme testosterone and DHT values were also excluded; seven had testosterone less than 20 ng/dl (0.69 nmol/liter) and DHT less than 6.0 ng/dl (0.21 nmol/liter), one had a testosterone value of 3710 ng/dl (128.64 nmol/liter), and two had DHT values greater than 500 ng/dl (17.34 nmol/liter).

[d] *P* value for difference in means on the log scale between the racial/ethnic groups.

[e] Metric units in nanograms per deciliter can be divided by 28.84 to obtain SI units, nanomoles per liter.

[f] Metric units in micrograms per deciliter can be multiplied by 0.02714 to obtain SI units, micromoles per liter.

and DHT to testosterone levels ($P = 0.077$). The best model to describe DHT to testosterone ratios adjusted for age, PASE, and hours blood taken from awakening; race/ethnicity had a significant effect in this model ($P = 0.038$). PASE had a negative relationship with DHT to testosterone and similar to before covariate adjustment, blacks had higher DHT to testosterone ratios, compared with whites ($P = 0.047$) and Hispanics ($P = 0.016$); no difference was found between Hispanics and whites ($P = 0.584$).

Unadjusted SHBG levels did not differ by race/ethnicity (Table 4), and in a model to predict SHBG values adjusting for age, the *P* value for the race/ethnicity covariate was 0.901 (Fig. 1E). After fitting the best multivariate model including age, WHR, BMI, smoking status, and time blood taken from awakening, the *P* value for the effect of racial/ethnic differences was 0.981; age and smoking were positively associated, whereas BMI and WHR were negatively associated with SHBG levels.

In unadjusted analysis, DHEAS values differed by racial/ethnic group (Table 4 where $P = 0.027$); however, in a model to predict DHEAS values adjusting for age, the *P* value for the race/ethnicity covariate was 0.121 (Fig. 1F). In a multivariate model including PCS12, drinking status, SES, and hours blood taken from awakening, there was no evidence of a racial/ethnic difference in DHEAS ($P = 0.586$). Age had a significant negative effect on DHEAS, whereas PCS12 and alcoholic drinking were positively associated with DHEAS levels.

Discussion

After adjusting for covariates such as age, anthropometric measures, and comorbid conditions that affect sex steroid levels, no statistically significant racial/ethnic differences in testosterone, bioavailable testosterone, SHBG, or DHEAS levels are found. However, there is some evidence of racial/ethnic differences in DHT levels and DHT to testosterone ratios after covariate adjustment. Men who describe themselves as blacks have the highest DHT levels and DHT to testosterone ratios, compared with those who describe themselves as Hispanics or whites. The significant correlations between total testosterone and bioavailable testosterone levels, total testosterone and SHBG concentrations, and bioavailable testosterone and age provide evidence of internal consistency as well as biological plausibility of these data (48–50). In addition, bioavailable testosterone concentrations are not significantly correlated with SHBG, providing a valid, SHBG-independent marker of circulating testosterone.

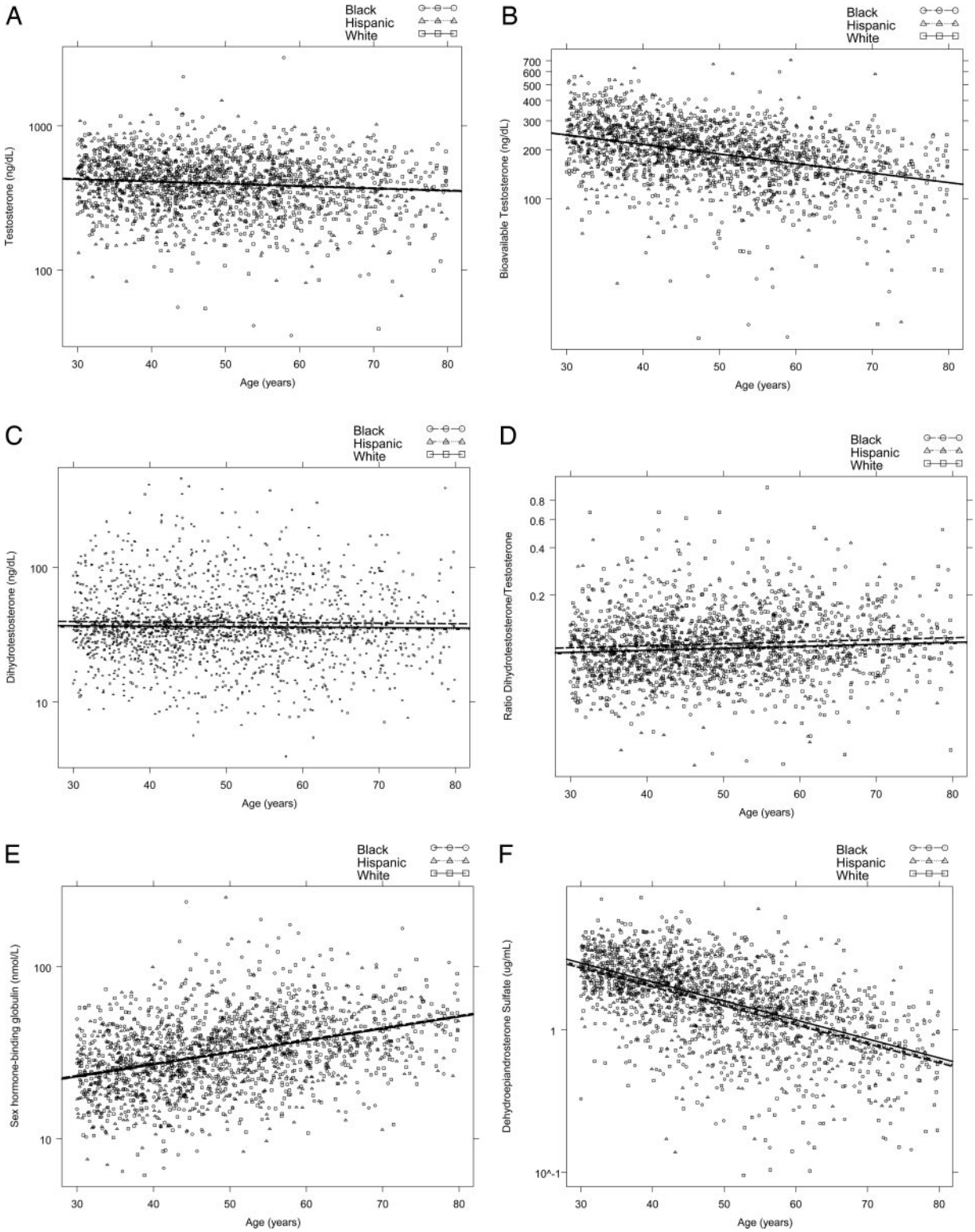

FIG. 1. Androgen values on the log scale from the BACH Survey (2002–2005) *vs.* age (30–79 yr) by racial/ethnic group (black, Hispanic, white). A, Testosterone (nanograms per deciliter). B, Bioavailable testosterone (nanograms per deciliter). C, DHT (nanograms per deciliter). D, Ratio of DHT to testosterone. E, SHBG (nanomoles per liter). F, DHEAS (micrograms per milliliter). Metric units in nanograms per deciliter can be divided by 28.84 to obtain SI units, nanomoles per liter. Metric units in micrograms per deciliter can be multiplied by 0.02714 to obtain SI units, micromoles per liter.

Our findings have several clinical implications. Because total and bioavailable testosterone concentrations do not differ among men of different racial/ethnic groups, the normative ranges for total testosterone and bioavailable testosterone concentrations need not be adjusted for race/ethnicity when establishing the diagnosis of androgen deficiency syn-

TABLE 5. Multivariate linear regression model from the BACH Survey (2002–2005) to determine whether there are racial/ethnic differences in log DHT levels (nanograms per deciliter)[a] controlling for age at baseline, BMI, and hours blood taken from awakening

	Estimate	SE	Wald F test[b] *P* value	Individual *t* test *P* values
Intercept	1.6772	0.0404	<0.001	
Age at baseline	0.000103	0.000668	0.877	
Race/ethnicity			0.047	
Black	0.0405	0.0187		0.034,[c] 0.031[d]
Hispanic	−0.0043	0.0199		0.829[d]
White	0	Reference		
BMI			<0.001	
<25 kg/m^2	0	Reference		
25–29 kg/m^2	−0.0827	0.0210		<0.001[e]
30+ kg/m^2	−0.1896	0.0220		<0.001,[f] <0.001[e]
Hours blood taken from awakening	−0.0062	0.00269	0.021	

[a] DHT in nanograms per deciliter can be divided by 28.84 to obtain SI units, nanomoles per liter.
[b] The Wald F test quantifies whether log DHT levels vary according to the covariate; the individual *t* tests compare the categories within categorical variables.
[c] Compared with Hispanics.
[d] Compared with whites.
[e] Compared with BMI less than 25 kg/m^2.
[f] Compared with BMI 25–29 kg/m^2.

dromes in men aged 30–79 yr . Although polymorphisms in the testosterone biosynthetic pathway have been postulated (51), especially in the CYP17 gene, our data do not support the hypothesis that genetic differences in pathways that contribute to circulating testosterone levels could explain racial/ethnic disparities in prostate cancer incidence rates.

We found higher DHT levels and DHT to testosterone ratios in black men than Hispanics and whites. We do not know whether these small but significant differences in DHT levels and DHT to testosterone ratios can account for the observed racial/ethnic variations in prostate cancer incidence and mortality rates. Others (9, 15, 16) have examined racial/ethnic differences in the DHT to testosterone ratio or testosterone conversion rates as indirect markers for racial/ethnic differences in the steroid 5α-reductase activity; these studies have generally reported lower steroid 5α-reductase activity in Chinese (16) and Japanese (7) men than white and black men. Testosterone's effects on the prostate are mediated through its conversion to DHT by the action of steroid 5α-reductase type II (SRD5A2). Polymorphisms in SRD5A2 have been associated with benign prostatic hyperplasia and prostate cancer (52, 53); these polymorphisms might alter tissue levels of DHT and could increase prostate cancer risk. Further research is needed to determine whether higher DHT levels and DHT to testosterone ratios in black men are due to polymorphisms in SRD5A2 gene and whether these small differences can explain the racial disparities in prostate cancer incidence and prevalence rates.

Blacks have a greater propensity to form keloids (54), another disorder in which androgens have been invoked. Some testosterone effects on the skin are mediated through its conversion to DHT (55). However, it is not clear whether steroid 5α-reduction of testosterone is obligatory for mediating its effects on the skeletal muscle and bone. The SRD5A2 gene is expressed at a low level in the human skeletal muscle and bone. 46,XY individuals with congenital mutations of the SRD5A2 gene undergo normal muscular and bone development at puberty (55). Furthermore, men treated with SRD5A2 inhibitors for the treatment of benign prostatic hyperplasia do not experience loss of skeletal muscle mass or bone mineral density, suggesting that 5α-reduction of testosterone to DHT is not obligatory for mediating its anabolic effects on the muscle and the bone (56). Additional mechanisms, other than small differences in DHT levels, may need to be invoked to explain the racial/ethnic differences in body composition and fracture rates.

Racial/ethnic differences in tissue androgen concentrations might exist because of variations in tissue metabolism of testosterone (57). Differences in androgen signaling pathways that may affect tissue-specific effects of testosterone have been suggested to contribute to racial/ethnic differences in prostate cancer risk. For instance, the androgen

TABLE 6. Comparison of linear regression models from the BACH Survey (2002–2005) to determine whether there are racial/ethnic differences in log DHT levels (nanograms per deciliter)[a]

Variables in the model	Race/ethnicity coefficient (SE) for black men	Race/ethnicity coefficient (SE) for Hispanic men	*P* value Wald F test[b]
Race/ethnicity only	0.0319 (0.0194)	−0.0080 (0.0201)	0.121
Race/ethnicity, age	0.0318 (0.0194)	−0.0093 (0.0206)	0.119
Race/ethnicity, age, hours from waking	0.0319 (0.0192)	−0.0060 (0.0207)	0.143
Race/ethnicity, age, hours from waking, WHR	0.0144 (0.0190)	−0.0051 (0.0201)	0.628
Race/ethnicity, age, hours from waking, BMI[c]	0.0405 (0.0187)	−0.0043 (0.0199)	0.047
Race/ethnicity, age, hours from waking, WHR, BMI	0.0313 (0.0189)	−0.0046 (0.0199)	0.160

[a] DHT in nanograms per deciliter can be divided by 28.84 to obtain SI units, nanomoles per liter.
[b] The Wald F test quantifies whether log DHT levels vary according to race/ethnicity. White men are considered the reference category with a race/ethnicity coefficient of 0.
[c] This model was deemed the best model and is presented in full in Table 5.

receptor expression is higher in the prostatectomy samples of black men with and without prostate cancer in comparison with those from white men (58). Polymorphisms in the signaling cascades downstream of androgen receptors have not been studied. The BACH Survey was not designed to evaluate tissue androgen metabolism or signal transduction pathways.

To our knowledge, this is the first survey of racial/ethnic variations in androgen levels that included many men of Hispanic origin. However, significant dietary and cultural differences within each racial/ethnic group across different geographic regions may exist. This is especially true of Hispanics in the Boston area who differ from those in the southeastern and western states in their countries of origin and sociocultural and dietary patterns (Office of Minority Health, www.omhrc.gov). A recent study of older men (59) demonstrated racial/ethnic differences in total testosterone (adjusting for BMI, age) with significantly lower levels in Asian men, compared with white, black, and Hispanic men. Subjects were recruited through six U.S. academic medical centers; therefore, this Hispanic population may differ from Boston Hispanics. Our racial/ethnic categories are defined by an individual's self-selection, a widely accepted and used method (60), but the effects of race/ethnicity might be diluted due to interracial marriage, cultural assimilation, and other factors. Finally, we recognize that genetic factors that contribute to the observed differences in body composition, bone mass, and susceptibility to disease (18, 35) may interact with multiple environmental and host factors, most of them poorly understood and not studied in the BACH Survey.

In summary, our data do not demonstrate significant differences in total testosterone, bioavailable testosterone, SHBG, or DHEAS levels among white, black, and Hispanic men in a large, community-based sample of Boston men after adjusting for age, anthropometric measures, and comorbid conditions. We, however, found small but significant differences in DHT levels and DHT to testosterone ratios after covariate adjustment. Our data suggest that the normative ranges for total testosterone and bioavailable testosterone concentrations need not be adjusted for race/ethnicity when establishing the diagnosis of androgen deficiency syndromes in men aged 30–79 yr. The genetic basis and clinical significance of the higher DHT levels and DHT to testosterone ratios among blacks, compared with whites and Hispanics, should be further explored to ascertain whether they can explain racial/ethnic differences in androgen-related clinical disorders, body composition, and bone density.

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Address all correspondence and requests for reprints to: Heather J. Litman, Research Scientist, New England Research Institutes, 9 Galen Street, Watertown, Massachusetts 02472. E-mail: hlitman@neriscience.com.

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