# Assessing the vitamin D status of the US population<sup>1-4</sup>

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## ABSTRACT

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This article describes the information currently available in the National Nutrition Monitoring System that is relevant to assessing the vitamin D status of US population groups, the strengths and limitations of this information, and selected results of vitamin D nutritional status assessments. The National Health and Nutrition Examination Survey (NHANES) provides information on vitamin D intakes only from 1988 to 1994. NHANES collected information on supplement use and circulating 25-hydroxyvitamin D [25(OH)D] concentrations from 1988 through current surveys. The National Nutrient Database for Standard Reference started providing limited data on the vitamin D content of foods in 2002 and continues to update these values. The Food Label and Package Survey provides 2006-2007 label information on vitamin D fortification of marketed foods. Despite limitations in the available data and controversies about appropriate criteria for evaluating vitamin D status among population groups, we can make some useful comparisons of vitamin D status among lifestage groups. In general, males have higher vitamin D intakes and 25(OH)D concentrations than do females. Children tend to have higher vitamin D status than adults. The increasing use of multivitamin-mineral dietary supplements in younger to older adults is not associated with a corresponding increase in serum 25(OH)D concentrations. In general, leaner individuals have higher circulating concentrations of 25(OH)D and supplement use than do heavier individuals. Finally, non-Hispanic whites tend to have higher vitamin D status than do non-Hispanic blacks and Mexican Americans. Am J Clin Nutr 2008;88(suppl):558S-64S.

# INTRODUCTION

The purpose of this article is to describe the availability of data for assessing the vitamin D nutritional status of US population groups and selected results of vitamin D status assessments by using data from the National Nutrition Monitoring System (NNMS). Surveys and related databases in the NNMS provide information about the nutrition-related health status of Americans over time and reference information on the nutrient composition of foods and dietary supplements (1). Shown in Table 1 is relevant vitamin D information collected by the National Health and Nutrition Examination Survey (NHANES) conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC; 2-14), the National Nutrient Database for Standard Reference (NNDB) developed by the Nutrient Data Laboratory of the US Department of Agriculture (USDA; 15), and the Food Label and Package Survey (FLAPS) conducted by the Center for Food Safety and Applied Nutrition of the Food and Drug Administration (CF-SAN/FDA; personal communication, Mary Brandt, CFSAN/FDA, 2007).

When using national databases, documentation of data quality and interpretability of nutritional variables are critical issues (1, 13, 16–18). In addition, for NHANES and other national surveys, the ability to obtain meaningful results depends on the use of statistical software to address the complex sampling designs (16, 17). Statistical adjustments for converting data from dietary recalls into usual intakes are also necessary to avoid misleading the users of the data by providing inflated estimates at the tails of the distribution curves (19).

## VITAMIN D INTAKES

Intake estimations require information on the vitamin D content of foods and supplements and the frequency, types, and amounts of foods and supplements consumed.

### Vitamin D content of foods

The USDA first published data on the vitamin D content of foods in a provisional table in 1991 and issued updates in 1999 (20). Since 2002, and most recently in September 2007, the USDA has incorporated these data and their updates into the annual public releases of the USDA's NNDB for Standard Reference (15). However, these databases have incomplete vitamin D content information, with data available for only 594 of 7519 foods in the 2007 release. The sources of vitamin D information in the database include analytic values, label declarations for many processed foods, literature values, and calculated values based on ingredient composition.

The food industry is increasingly marketing foods fortified with vitamin D. The FDA provided preliminary results on the vitamin D-related label information from the processed, packaged food products included in the 2006–2007 FLAPS. The 2006–2007 FLAPS is the latest in a series of surveys conducted

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<sup>&</sup>lt;sup>3</sup> The opinions in this article are those of the author and do not necessarily represent official opinions or positions of the US federal government, the Department of Health and Human Services, or the National Institutes of Health.

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#### TABLE 1

Data in the National Nutrition Monitoring System that can be used to assess the vitamin D status of US population groups<sup>I</sup>

Relevant vitamin D data	Database	
Circulating concentrations of 25(OH)D	NHANES (1988–1994; 2000 <sup>2</sup> –2004)	
Vitamin D intakes from foods	NHANES III (1988–1994)	
Vitamin D: use of and intakes from dietary supplements	NHANES (1988–1994; 1999–2006 <sup>3</sup> )	
Vitamin D content of foods	NNDB (2002–2007)	
Vitamin D label content of dietary supplements	NHANES (1988–1994; 1999–2006 <sup>3</sup> )	
Vitamin D label information on packaged and processed foods	FLAPS (2006–2007) <sup>4</sup>	

<sup>1</sup> 25(OH)D, 25-hydroxyvitamin D; NHANES, National Health and Nutrition Examination Survey; NNDB, National Nutrient Database for Standard Reference; FLAPS, Food Label and Package Survey.

<sup>2</sup> 2000 data available only from the Research Data Center, National Center for Health Statistics, Centers for Disease Control and Prevention.

<sup>3</sup> 2005–2006 data will be publicly available in 2008.

<sup>4</sup> Preliminary data only based on personal communication from Mary Brandt, Center for Food Safety and Applied Nutrition, US Food and Drug Administration, 2007.

periodically over the past 30 y (21). It consists of a nationally representative sample of >1200 food products selected from the AC Nielsen food marketing database by using a probability-based random sampling technique.

The 2006–2007 FLAPS data suggest that almost all fluid milks,  $\approx$ 75% of ready-to-eat breakfast cereals, slightly more than half of all milk substitutes, approximately one-fourth of yogurts, and  $\approx$ 8–14% of cheeses, juices, and spreads are fortified with vitamin D (personal communication, Mary Brandt, CFSAN/FDA, 2007). Many product labels included in the survey indicated that the form of added vitamin D was vitamin D<sub>3</sub>. However, some milk substitutes are fortified with vitamin D<sub>2</sub>. The ready-to-eat cereal labels did not specify the form of added vitamin D. Levels of vitamin D ranged from 1  $\mu$ g (40 IU) per regulatory serving for ready-to-eat cereals and cheeses to 1.5  $\mu$ g (60 IU) for spreads and 2.5  $\mu$ g (100 IU) for fluid milks. Several food categories (eg, juices and drinks, milk substitutes, and yogurts) had within-category ranges of 1 to 2.5  $\mu$ g (40 to 100 IU) of vitamin D per regulatory serving.

Human milk or commercial infant formula constitutes the sole source of nutrition for the first few months of life. On average, human milk contains  $\approx 0.14 \ \mu g$  (5.7 IU) vitamin D<sub>3</sub> per 100 kcal (22). However, its biological activity is higher than the analyzed values indicate because human milk contains 25-hydroxyvitamin D [25(OH)D] in addition to vitamin D<sub>3</sub> (23), and the analyzed value does not include the 25(OH)D content. In addition, the biological activity of 25(OH)D is higher than that of vitamin D. Commercial infant formulas contain  $\approx 1.5 \ \mu g$  (60 IU) per 100 kcal in the NNDB (24). These levels are close to the midpoint in the range that the FDA regulations have established for commercially available infant formula, which must contain between 1  $\mu g$  (40 IU) and 2.5  $\mu g$  (100 IU) of vitamin D per 100 kcal (25).

The accuracy of label information on the vitamin D content of infant formulas is controversial. A 1992 publication suggested that the vitamin D content of 7 of 10 commercial infant formulas

exceeded label declarations by >200%, with one product containing >400% of its label value (26). More recently, the FDA used the American Association of Analytic Chemists' Official Method no. 992.26 for vitamin D in milk-based infant formulas (27, 28) to analyze >80 commercial milk-based infant formulas collected between 2003 and 2006. The results showed that products contained 87–184% of label declarations (personal communication, Jeanne Rader, CFSAN/FDA, 2007).

#### Vitamin D content of dietary supplements

Since 1988, NHANES has collected label information on dietary supplements, including vitamin D, used by study participants (11–14, 18). An ongoing study is developing a dietary supplement composition database that will provide analyzed values for selected nutrients in the top marketed multivitaminmineral supplement products (29-31). A standard reference material for fat-soluble and other nutrients in a multivitaminmineral dietary supplement will soon be available (32).

Traditionally, many marketed dietary supplements contained 400 IU per daily dose. The form of vitamin D used in supplement products can be either vitamin  $D_2$  or vitamin  $D_3$ . A quick scan of currently marketed products suggests that some manufacturers are switching their vitamin D source from vitamin  $D_2$  to vitamin  $D_3$  and some are increasing the vitamin D content of their products (eg, from 400 to 800 IU or more per day).

#### Label values as surrogates for vitamin D content

In the absence of analyzed values for the vitamin D content of foods and supplements, label declarations of amounts of vitamin D are often used as surrogates of vitamin D content. In the United States, label values that comply with FDA regulations generally underestimate the actual amount of vitamin D (or any other vitamin) because they must reflect the minimum amount of vitamin D in the product throughout its shelf life (18). To ensure that their products meet FDA regulatory requirements, manufacturers tend to add overages to fortified foods. A dietary supplement trade association recently suggested that manufacturers of dietary supplements add overages of  $\approx 30-50\%$  of vitamin D<sub>2</sub> and 30% of vitamin  $D_3$  to dietary supplement products (18). For naturally occurring sources of vitamin D in foods, manufacturers must declare the minimum level after taking into account shelf life losses and natural variabilities in content. Because other countries (eg, in Europe, Canada) require that manufacturers base label nutrient declarations on means rather than minimums, the meaning of label declarations varies from country to country.

The accuracy of label declarations of vitamin D in foods is also uncertain because of the paucity of validated analytic methods for a broad range of food matrices and the absence of standard reference materials for analyzing the vitamin D content of foods, except for milk-based infant formulas (33, 34). In 1992, Holick et al (26) reported that only 29% of 42 milk samples contained 80-120% of the vitamin D label declaration, 62% of the milk samples contained <80% of the claimed label value, and 3 of 14 samples of skim milk contained no detectable vitamin D. Tanner et al (35) suggested that the decreasing adherence to the label claim with decreasing fat content in fortified milks in the 1980s could have been due to methods and stage of vitamin addition before processing. More recently, a 4-y survey of fluid milks in New York suggested that approximately half complied with label declarations (36). Most milk samples that were out of compliance were underfortified, and the content of slightly <20% of underfortified products was within 20% of the label claim, although vitamin D concentrations did not vary by milk fat content.

Given the uncertainties about the accuracy of analytic methods, the lack of standard reference materials for most food matrices, the incompleteness of fortification data on nationally representative food products, and the dated nature of many of the published analytic results, determining the usefulness of vitamin D label values for estimating intakes remains difficult.

#### Intake data

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Because of unresolved problems in obtaining accurate and complete information on the vitamin D content of foods, the USDA did not include vitamin D composition data from the NNDB when they developed the survey food-composition files for the 1999 to the current NHANES. NHANES III (1988– 1994), which used vitamin D composition data from the University of Minnesota database, is the only national survey database that provides information on the vitamin D content of foods as part of the survey documentation (Table 1; 7).

Calvo et al (10) estimated vitamin D intakes for US population groups by using the NHANES III (1988-1994) data. They applied statistical adjustments to estimate usual intakes and to account for the complex sampling design used in NHANES. This survey is dated, the adequacy of the composition databases is uncertain, and dietary intakes generally tend to have an underreporting bias (37, 38); however, the NHANES III data can provide useful information on relative differences among subgroups and underscore the importance of including dietary supplement use in estimates of total intakes. Calvo et al found that males generally had a higher intake than did females (Table 2). Moore et al (39), also using the NHANES III survey, found that total intake of vitamin D was lowest in females aged 14-30 y and highest in children aged 1-8 y. Estimates from a later NHANES (1999-2000) in which the authors updated earlier vitamin D composition files, suggested that females aged  $\geq 51$  y had the highest total intake (9.5  $\pm$  0.4  $\mu$ g/d, or 380  $\pm$  16 IU) and females aged 9–18 y had the lowest total intake [5.6  $\pm$  0.3  $\mu$ g/d, or 224  $\pm$  12 IU (40)]. In both NHANES III (1988–1994) and the 1999– 2000 NHANES surveys, non-Hispanic whites generally had a higher intake than did non-Hispanic blacks and Mexican-Americans (Table 2; 10, 40). Estimated mean total intakes (from foods and supplements) were  $\approx 20-40\%$  higher than mean intakes from foods alone in NHANES III (10). In general, means were higher than medians for all groups. This suggests a significant skew to the intake distributions and indicates that some persons had a relatively high total intake (10).

#### Prevalence of supplement use

Because dietary supplements contain relatively large amounts of nutrients in concentrated form, supplement use can markedly affect total intakes of micronutrients. NHANES has collected information on dietary supplement use and label declarations of nutrient content since 1988 (Table 1). Over time, dietary supplement use has increased among adults (12) but has remained relatively constant or declined in children; declines are most pronounced in younger children (11). Multivitamin-multimineral supplements are the most common supplement product consumed by both adults and children.

In NHANES 1999–2002, the percentage of children taking vitamin D-containing supplements ranged from 9% for children

#### TABLE 2

Usual total vitamin D intake (from foods and supplements), third National Health and Nutrition Examination Survey, 1988-1994<sup>1</sup>

Group	Females	Males
	μg/d (IU/d)	
6–11 y		
Non-Hispanic whites	$8.09 \pm 0.283$	$9.58 \pm 0.336$
	$(323.6 \pm 11.32)$	$(383.2 \pm 13.44)$
Non-Hispanic blacks	$8.27 \pm 0.296$	$7.45 \pm 0.174$
	$(330.8 \pm 11.84)$	$(298.0 \pm 6.96)$
Mexican Americans	$8.01 \pm 0.256$	$8.54 \pm 0.486$
	$(320.4 \pm 10.24)$	$(341.6 \pm 19.44)$
12–19 y	· · · · · ·	· · · · · · · · · · · · · · · · · · ·
Non-Hispanic whites	$6.47 \pm 0.283$	$8.43 \pm 0.429$
	$(258.8 \pm 11.32)$	$(337.2 \pm 17.16)$
Non-Hispanic blacks	$5.24 \pm 0.219$	$6.74 \pm 0.412$
	$(209.6 \pm 8.76)$	$(269.6 \pm 16.48)$
Mexican Americans	$5.94 \pm 0.257$	$7.36 \pm 0.420$
	$(237.6 \pm 10.28)$	$(294.4 \pm 16.80)$
20–49 у		
Non-Hispanic whites	$7.33 \pm 0.262$	$8.12 \pm 0.335$
	$(293.2 \pm 10.48)$	$(324.8 \pm 13.40)$
Non-Hispanic blacks	$5.73 \pm 0.196$	$6.90 \pm 0.236$
	$(229.2 \pm 7.84)$	$(276.0 \pm 9.44)$
Mexican Americans	$5.69 \pm 0.264$	$6.16 \pm 0.209$
	$(227.6 \pm 10.56)$	$(246.4 \pm 8.36)$
≥ 50 y		
Non-Hispanic whites	$8.37 \pm 0.319$	$8.11 \pm 0.212$
	$(334.8 \pm 12.76)$	$(324.4 \pm 8.48)$
Non-Hispanic blacks	$5.94 \pm 0.286$	$5.96 \pm 0.279$
	$(237.6 \pm 11.44)$	$(238.4 \pm 11.16)$
Mexican Americans	$5.95 \pm 0.291$	$6.13 \pm 0.244$
	$(238.0 \pm 11.64)$	$(245.2 \pm 9.76)$

<sup>1</sup> All values are *mean*  $\pm$  SEM. Adapted from Calvo et al, 2004 (10).

younger than 1 y to 36% for children aged 4-8 y (11). The prevalence of vitamin D supplement use was 33% in children aged 1–3 y, 23% in those aged 9–13 y, and 16% in adolescents aged 14–18 y. Overall, males and females had a similar prevalence of use (25% of males and 27% of females). Non-Hispanic white children had a higher prevalence of use (31%) than did non-Hispanic black (16%) and Mexican American children (19%). Children classified as being underweight or at risk of underweight had a higher prevalence of use of vitamin D–containing supplements (30% for underweight children, 32% for children at risk of underweight) than did children classified as probably being at a healthy weight (28%), at risk of overweight (23%), or overweight (20%).

Radimer et al (12) published results on the prevalence of multivitamin-multimineral supplement use in adults from NHANES 1999–2000 but did not provide specific information on the use of vitamin D–containing dietary supplements. They reported a prevalence of multivitamin-multimineral use of 32% in males and 38% in females. Multivitamin-multimineral use increased with age from 30% for adults aged 20–39 y to 40% for adults aged  $\geq 60$  y. As with children, a larger percentage of non-Hispanic white adults (40%) than non-Hispanic blacks (23%) or Mexican Americans (20%) used multivitamin-multimineral supplements. Similarly, leaner adults were more likely to use multivitamin-multimineral supplements than were obese adults [40% among those with a body mass index (BMI; in

kg/m<sup>2</sup>) <25.0, 34% with a BMI of 25.0 to <30.0, and 30% with a BMI of  $\geq$ 30.0].

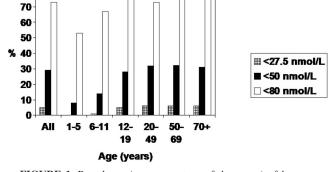
## VITAMIN D STATUS

NHANES collects and analyzes biomarkers and clinical measures of nutritional and other health status indicators through direct standardized physical examinations and laboratory analysis. Since 1988, NHANES has included data on serum 25(OH)D concentrations for persons 12 y or older (2–9). NCHS extended the NHANES data collection to include children older than 6 y in 2000 and to children 1 y or older in 2003. NHANES 2000–2004 has data on 25(OH)D concentrations from >20 000 persons.

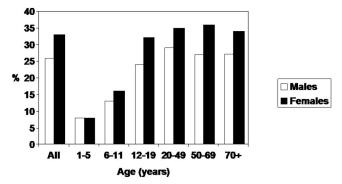
A major strength of NHANES is its estimation of population groups at risk of nutritional insufficiency. CDC's National Center for Environmental Health used the DiaSorin radioimmunoassay kit (DiaSorin Inc, Stillwater, MN) to provide data on serum 25(OH)D concentrations for NHANES (2-3, 41). The CDC's NCHS used these results to provide information on serum 25(OH)D concentrations in US population groups for the Vitamin D and Health in the 21st Century conference (personal communication, Anne Looker, NCHS/CDC, 2007). Prevalence estimates for various age groups are shown in Figure 1. I present 3 cutoffs for serum 25(OH)D concentrations because of the controversy regarding the definition of vitamin D insufficiency (23, 42-44). NCHS found that 5% of NHANES participants had values below the traditional cutoff of < 27.5 nmol/L (11 ng/mL). The prevalence of values < 27.5 nmol/L was  $\le 1\%$  for infants and children aged  $\leq 11$  y, 5% for adolescents aged 12–19 y, and 6% for adults aged  $\geq 20$  y. The use of higher cutoffs resulted in considerably higher prevalence rates of low 25(OH)D values.

Differences in 25(OH)D concentrations between males and females by age group are shown in **Figure 2**. Except for children aged 1–5 y, females had a higher prevalence of low 25(OH)D concentrations than did males. The prevalence of serum 25(OH)D concentrations <50 nmol/L was  $\approx$ 30% higher in non-pregnant than in pregnant women (data not shown).

Differences in mean serum 25(OH)D concentrations for 3 racial/ethnic groups are shown in **Figure 3**. Non-Hispanic whites tended to have higher concentrations than did non-Hispanic blacks. Mexican Americans had concentrations intermediate between these 2 groups. This rank order of differences held across all age groups.



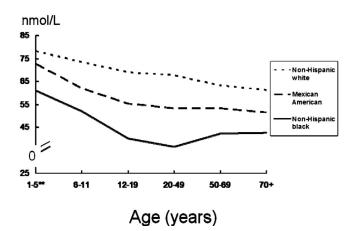
**FIGURE 1.** Prevalence (as a percentage of the group) of low serum 25-hydroxyvitamin D concentrations from the National Health and Nutrition Examination Survey (NHANES) 2000–2004 by cutoff. Data for ages 1–5 y are available from NHANES 2003–2004 only.



**FIGURE 2.** Prevalence (as a percentage of the group) of a serum 25hydroxyvitamin D concentration <50 nmol/L for men ( $\Box$ ) and women ( $\blacksquare$ ) from the National Health and Nutrition Examination Survey (NHANES) 2000–2004. Data for ages 1–5 y are available from NHANES 2003–2004 only.

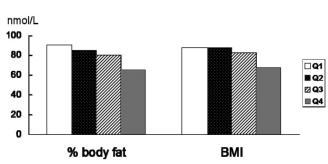
NHANES data indicate an inverse relation between measures of body fat or BMI and serum 25(OH)D concentrations (8, 45). The association between 2 different measures of body fat or leanness and serum 25(OH)D concentrations for non-Hispanic white females aged 20-49 y from NHANES III (1988-1994) are shown in Figure 4 (personal communication, Anne Looker, NCHS/CDC, 2007). Regardless of the measures used, leaner women had a higher serum 25(OH)D concentration than did heavier women. Although not shown, the most physically active women had the highest serum 25(OH)D concentration and the least active women had the lowest. Further analyses found that differences in physical activity could account for some but not all differences in serum 25(OH)D concentration by body fat value. However, the inverse relation between obesity and serum 25(OH)D concentrations appears to vary by race: the relation is weaker in non-Hispanic black women than in non-Hispanic white women (8).

The factors that affected serum 25(OH)D concentrations in women aged 15–49 y in NHANES III included milk or cereal consumption, use of vitamin D supplements, season, urban residence, and use of oral contraceptive pills (46).



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**FIGURE 4.** Serum 25-hydroxyvitamin D [25(OH)D] concentration from the National Health and Nutrition Examination Survey (NHANES) 1988– 1994 by body fat quartile (Q) for non-Hispanic white women aged 20–49 y. Serum 25(OH)D means are age-adjusted. Percentage body fat is estimated from bioelectrical impedance. The relation between serum 25(OH)D concentration and both body fat and body mass index was highly significant (P = 0.000).

#### EVALUATING SUFFICIENCY

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I have described the available data and selected results from the NNMS that are relevant to evaluating the vitamin D nutritional status of US population groups. I have attempted to follow the approaches that expert panels (1) identified; these approaches emphasized the need to consider both data quality and interpretability issues when using the NNMS data for assessing the nutritional status of the US population. Current evaluations of the vitamin D status of US population groups warrant caution due to uncertainties regarding the completeness, measurement techniques, and interpretability of currently available dietary and biomarker status measures.

The use of 25(OH)D concentrations as a biomarker of vitamin D exposure and status is common (23, 44). 25(OH)D concentrations reflect the net effects of cutaneous synthesis from sun exposure and oral intake from food and supplement sources, with correction for potential differences in the bioavailability and bioequivalence of these different sources and differences in skin bioconversion rates. However, scientists should be cautious when interpreting data on 25(OH)D concentrations, because laboratory methods lack standardization (44, 47, 48). Even the subtle methodologic drift that occurred when CDC used the Dia-Sorin radioimmunoassay for analyzing NHANES 25(OH)D concentrations from 1988 through 2004 (41) illustrates the need to be aware of the uncertainties surrounding the use of 25(OH)D concentration as a measure of vitamin D sufficiency. A standard reference material for serum 25(OH)D should be available soon and will enhance our ability to ensure accuracy and comparability of results (49).

In 1997, a US expert panel considered a 25(OH)D concentration of  $\geq$ 27.5 nmol/L as an indicator of adequate vitamin D status from birth through 18 y and a concentration of  $\geq$ 30 nmol/L for adults aged 19–50 y (23). The panel based these values on their associations with linear growth and bone mass in infants, the absence of signs and symptoms of vitamin D deficiency in children, and the relation of 25(OH)D with parathyroid hormone concentrations and calcium balance in adults aged 19-50 y. The panel used bone health and prevention of bone loss in conjunction with relations between parathyroid hormone and 25(OH)D concentrations as indicators of adequate vitamin D status for adults  $\geq$ 51 y. In 2007, a UK expert panel considered a plasma concentration of <25 nmol/L as an index of suboptimal vitamin D status (44). They stated that vitamin D deficiency results in rickets and osteomalacia. Based on the midpoint in the range of values used in the 2 reports described above, the NHANES 2000–2004 data show that  $\approx$ 1–9% of the US population has 25(OH)D concentrations <27.5 nmol/L; adults have the highest and children have the lowest risk.

Recently, several researchers used results from randomized clinical trials to compare serum 25(OH)D concentrations in persons aged  $\geq 65$  y with the incidence of nonvertebral or hip fractures; they suggested that 25(OH)D thresholds of 50-80 nmol/L are optimal indicators of adequate vitamin D status (42). Because of the lack of randomized clinical trials in other age and life-stage groups, several researchers have used results from crosssectional and cohort observational studies to suggest that a similar threshold 25(OH)D concentration is useful for identifying vitamin D insufficiency in younger adults (50). However, a recent systematic review concluded that, although fair evidence exists for an association between circulating 25(OH)D concentrations and some bone health outcomes (established rickets, parathyroid hormone concentration, falls, and bone mineral density), defining specific thresholds of circulating 25(OH)D for optimal bone health is difficult because of the imprecision of different 25(OH)D assays (51).

Noting these types of uncertainties, a scientific advisory committee commissioned by several UK government agencies concluded in a recent position paper that the current data are insufficient to clarify relations among vitamin D intake, biochemical status, and chronic disease outcomes (44). Specifically, they noted the complex interactions among dietary calcium intake, parathyroid hormone concentrations, renal function, and turnover of vitamin D metabolites, as well as the variable effects of age and other factors on these interrelations. Thus, controversy currently exists with regard to interpretive criteria for 25(OH)D concentrations across the life cycle and among subgroups.

Interpreting data on 25(OH)D concentrations for obese and overweight persons is particularly challenging. The NHANES showed lower circulating concentrations of 25(OH)D among young adult obese non-Hispanic white women than their leaner counterparts (8, 45). Differences in physical activity partially explained these differences, but the relations appeared to be weaker among non-Hispanic blacks than non-Hispanic whites. Some of these differences might be due to physiologic factors. Obese persons had lower circulating 25(OH)D concentrations than did leaner persons after supplementation with vitamin D<sub>2</sub> and after exposure to ultraviolet radiation (52). However, overweight and obese persons in NHANES also reported lower use of multivitamin-multimineral supplements and vitamin D-containing dietary supplements than did leaner persons of the same age or sex group (11-12); these results suggest that low dietary exposures could also contribute to the lower 25(OH)D concentrations in overweight and obese people. The 2007 UK advisory committee report cited a need to better understand the effects of adiposity on circulating 25(OHD) concentrations and the implications of the relation between adiposity and 25(OH)D concentrations for vitamin D requirements (44).

Limited information is available on the vitamin D intakes of US population groups because of the incomplete information on the vitamin D content of foods currently available, the lack of validated analytic methods for a wide range of food matrices (33), and the absence of standard reference materials for ensuring the accuracy of analytic results (34). Monitoring vitamin D intakes from dietary supplements is somewhat easier because a composition database is available that contains label information collected since 1988 on the vitamin D content of supplements used by NHANES participants (11–14). The quality of the information on the vitamin D content of marketed dietary supplements should soon improve with the availability of a standard reference material for analyzing vitamin D content in dietary supplements (32) and with the results of an upcoming analysis of the vitamin D content of 35 top dietary supplement multivitamin-multimineral products (29–31).

Given the concerns about data quality and interpretability of status measures, comparisons of survey results against predetermined cutoffs to assess the adequacy of intakes and of 25(OH)D concentrations require multidisciplinary discussions and expertise that are beyond the scope of this article. However, comparisons of relative differences among subgroups could be informative because common measurement tools are used across the groups being compared. Males of all age groups generally had a higher 25(OH)D concentration and a slightly higher total intake of vitamin D (foods plus supplements) than did females. Children had the lowest prevalence of low 25(OH)D concentrations and children aged 6-11 y had a higher total intake (foods plus supplements) than did older children or adults. Children aged 4-8 y also had higher dietary supplement use than did children of other ages. Supplement use was 30% in adults aged 20-39 y and 40%in adults aged  $\geq 60$  y; total intake tended to be slightly higher in older adults than in younger adults. However, the prevalence of serum 25(OH)D concentrations of <50 nmol/L was relatively stable across all adults aged  $\geq 20$  y. Relative differences among racial and ethnic groups tended to be consistent across the different measures of vitamin D status. In general, non-Hispanic whites had higher 25(OH)D concentrations, dietary intake, and dietary supplement use than did Mexican Americans and non-Hispanic blacks.

# SUMMARY

In this article, I identified the information in the NNMS that scientists can use to assess the vitamin D status of US population groups and described the strengths and weaknesses of the available data. Because of limitations in data quality, completeness, and interpretability, determining the proportion of the US population that is vitamin D sufficient is complex and controversial. A recent advisory committee report from the United Kingdom did not recommend changing the traditional 25(OH)D concentration cutoffs for vitamin D sufficiency due to the uncertainties and inconsistencies in the current evidence. Conversely, several researchers recently proposed significant changes to the criteria for determining vitamin D status. The numerous uncertainties in evaluating the vitamin D status of US population groups will benefit from further dialogue among a broad range of qualified experts, including experts in vitamin D metabolism, nutritional assessment across the life cycle and during pregnancy and lactation, biostatics, and various chronic diseases.

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#### REFERENCES

- Life Sciences Research Office, Federation of American Societies for Experimental Biology for the Interagency Board for Nutrition Monitoring and Related Research. Third report on nutrition monitoring in the United States. Volume 1. Washington, DC: US Government Printing Office, 1995. Internet: http://www.cdc.gov/nchs/data/misc/nutri95\_1acc.pdf (accessed 4 October 2007).
- National Center for Health Statistics, Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey 2003-2004. Documentation, codebook, and frequencies. Laboratory component: vitamin D. Survey years: 2003-2004. September 2007. Internet: http://www.cdc.gov/nchs/data/nhanes/03\_04/l06vid\_c.pdf (accessed 8 October 2007).
- National Center for Health Statistics, Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey 2001-2002. Documentation, codebook, and frequencies. Laboratory component: vitamin D. Survey years: 2001 to 2002. September 2007. Internet: http://www.cdc.gov/nchs/data/nhanes/nhanes\_01\_02/l06vid\_b.pdf (accessed 8 October 2007).
- National Center for Health Statistics, Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey, NHANES 2003-2004. Internet: http://www.cdc.gov/nchs/about/major/ nhanes/nhanes2003-2004/nhanes03\_04.htm (accessed 8 October 2007).
- National Center for Health Statistics, Centers for Disease Control and Prevention. National Nutrition and Health Examination Survey, NHANES 2001-2002. Internet: http://www.cdc.gov/nchs/about/major/ nhanes/nhanes01-02.htm (accessed 8 October 2007).
- National Center for Health Statistics, Centers for Disease Control and Prevention. 1999–2000 National Health and Nutrition Examination Survey (NHANES). Internet: http://www.cdc.gov/nchs/about/major/ nhanes/nhanes99\_00.htm (accessed 8 October 2007).
- National Center for Health Statistics, Centers for Disease Control and Prevention. Third National Health and Nutrition Examination Survey data files, documentation, and SAS code. Internet: http://www.cdc.gov/ nchs/about/major/nhanes/nh3data.htm (accessed 8 October 2007).
- Looker AC. Body fat and vitamin D status in black versus white women. J Clin Endocrinol Metab 2005;90:635–40.
- Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. Bone 2002;30:771–7.
- Calvo MS, Whiting SJ, Barton CN. Vitamin D fortification in the United States and Canada: current status and data needs. Am J Clin Nutr 2004; 80(suppl):1710S–6S.
- Picciano MF, Dwyer JT, Radimer KL, et al. Dietary supplement use among infants, children, and adolescents in the United States, 1999-2002. Arch Pediatr Adolesc Med 2007;161:978–85.
- Radimer K, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: data from the National Health and Nutrition Examination Survey, 1999-2000. Am J Epidemiol 2004;160: 339–49.
- Radimer KL. Methodological issues in assessing dietary supplement use in children. J Am Diet Assoc 2005;105:703–8.
- Radimer KL. National nutrition data: contributions and challenges to monitoring dietary supplement use in women. J Nutr 2003;133:2003S– 7S.
- US Department of Agriculture, Agricultural Research Service. Composition of foods; raw, processed, prepared. USDA national nutrient database for standard reference, release 20. September 2007. Internet: http:// www.ars.usda.gov/ba/bhnrc/ndl (accessed 8 October 2007).
- Yetley E, Johnson C. Nutritional applications of the Health and Nutrition Examination Surveys (HANES). Annu Rev Nutr 1987;7:441–63.
- Wright JD, Borrud LG, McDowell MA, Wang C-Y, Radimer K, Johnson CL. Nutrition assessment in the National Health and Nutrition Examination Survey 1999-2002. J Am Diet Assoc 2007;107:822–9.

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- Yetley EA. Multivitamin and multimineral dietary supplements: definitions, characterization, bioavailability, and drug interactions. Am J Clin Nutr 2007;85(suppl):269S–76S.
- Carriquiry AL. Estimation of usual intake distributions of nutrients and foods. J Nutr 2003;133:601S–8S.
- Weihrauch JL, Tamaki J. Provisional table on the vitamin D content of foods. US Department of Agriculture, Human Nutrition Information Service HNIS/PT-108, October 1991;slightly revised March 1999. Internet: http://www.nal.usda.gov/fnic/foodcomp/Data/Other/ vit\_d99.pdf (accessed 8 October 2007).
- LeGault L, Brandt MB, McCabe N, Adler C, Brown A-M, Brecher S. 2000-2001 Food label and package survey: an update on prevalence of nutrition labeling and claims on processed, packaged foods. J Am Diet Assoc 2004;104:952–8.
- US Department of Agriculture. National Nutrient Database for Standard Reference Release 20, NDB no. 01107. Milk, human, mature, fluid. Internet: http://www.ars.usda.gov/ba/bhnrc/ndl (accessed 8 October 2007).
- 23. Food and Nutrition Board. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Washington, DC: National Academy Press, 1997. Internet: http://fnic.nal.usda.gov/nal\_display/index.php?info\_center=4&tax\_level=4&tax\_subject=256&topic\_id=1342&level3\_id=5141&level4\_id=10587 (accessed 8 October 2007).
- 24. US Department of Agriculture. National Nutrient Database for Standard Reference release 20, NDB no. 03946. Infant formula, ROSS, SIMILAC LACTOSE FREE ADVANCE, ready-to-feed, with ARA and DHA; and NDB no. 03815 infant formula, MEAD JOHNSON, ENFAMIL LIPIL, with iron, ready-to-feed, with ARA and DHA. Internet: http://www. ars.usda.gov/ba/bhnrc/ndl (accessed 8 October 2007).
- Food and Drug Administration. Code of Federal Register Title 21, Sec. 107.100 Infant formula: nutrient specifications. Internet: http://www. accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm (accessed 8 October 2007).
- Holick MF, Shao Q, Liu WW, Chen TC. The vitamin D content of fortified milk and infant formula. N Engl J Med 1992;326:1178–81.
- Blake CJ. Committee on Food Nutrition. Fat-soluble vitamins. J AOAC Int 2005;88:325–9.
- Blake CJ. Status of methodology for the determination of fat-soluble vitamins in foods, dietary supplements, and vitamin premixes. J AOAC Int 2007;90:897–910.
- Dwyer JT, Holden J, Andrews K, et al. Measuring vitamins and minerals in dietary supplements for nutrition studies in the USA. Ann Bioanal Chem 2007;389:37–46.
- Dwyer JT, Picciano MF, Betz JM, et al. Progress in developing analytical and label-based dietary supplement databases at the NIH Office of Dietary Supplements. J Food Comp Anal 2008;21:S83–93.
- Roseland JM, Holden JM, Andrews KW, et al. Dietary supplement ingredient database (DSID): preliminary USDA studies on the composition of adult multivitamin/mineral supplements. J Food Comp Anal 2008;21:S69–77.
- 32. Sander LC, Sharpless KE, Wise SA. Dietary supplement standard reference materials. Life Sci 2006;78:2044–8.
- Byrdwell WC, DeVries J, Exler J, et al. Analyzing vitamin D in foods and supplements: methodologic challenges. Am J Clin Nutr 2008;88(suppl): 554S–7S.
- Sharpless KE, Greenberg RR, Schantz MM, Welch MJ, Wise SA, Ihnat M. Filling the AOAC triangle with food-matrix standard reference materials. Anal Bioanal Chem 2004;378:1161–7.

- Tanner JT, Smith J, Defibaugh P, et al. Survey of vitamin content of fortified milk. J Assoc Off Anal Chem 1988;71:607–10.
- Murphy SC, Whited LJ, Rosenberry LC, Hammond BH, Bandler DK, Boor KJ. Fluid milk vitamin fortification compliance in New York State. J Dairy Sci 2001;84:2813–20.
- 37. Schatzkin A, Kipnis V, Carroll RJ, et al. A comparison of a food frequency questionnaire with a 24-hour recall for use in an epidemiological cohort study: results from the biomarker-based Observing Protein and Energy Nutrition (OPEN) study. Int J Epidemiol 2003;32:1054–62.
- Briefel RR, McDowell MA, Alaimo K, et al. Total energy intake of the US population: the third National Health and Nutrition Examination Survey, 1988-1991. Am J Clin Nutr 1995;62(suppl):1072S–80S.
- Moore C, Murphy MM, Keast DR, Holick MF, Vitamin D intake in the United States. J Am Diet Assoc 2004;104:980–3.
- Moore CE, Murphy MM, Holick MF. Vitamin D intakes by children and adults in the United States differ among ethnic groups. J Nutr 2005;135: 2478–85.
- 41. Chen H, McCoy LF, Schleicher RL, Pfeiffer CM. Measurement of 25 hydroxyvitamin  $D_3$  (250H  $D_{33}$ ) and 25 hydroxyvitamin  $D_2$  (250H  $D_2$ ) in human serum using liquid chromatography-tandem mass spectrometry and its comparison to a radioimmunoassay method. Clin Chim Acta 2008;391:6–12.
- Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. Osteoporos Int 2005;16:713–6.
- Norman AW, Bouillon R, Whiting SJ, Vieth R, Lips P. 13<sup>th</sup> Workshop consensus for vitamin D nutritional guidelines. J Steroid Biochem Mol Biol 2007;103:204–5.
- 44. Scientific Advisory Committee on Nutrition. Update on vitamin D. Position statement. London: The Stationary Office Limited, 2007. Internet: http:// www.sacn.gov.uk/pdfs/sacn\_position\_vitamin\_d\_2007\_05\_07.pdf (accessed 7 November 2007).
- Looker AC. Do body fat and exercise modulate vitamin D status? Nutr Rev 2007;65:S124-6.
- 46. Nesby-O'Dell S, Scanlon KS, Cogswell ME, et al. Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: third National Health and Nutrition Examination Survey, 1988-1994. Am J Clin Nutr 2002;76:187–92.
- Binkley N, Krueger D, Cowgill CS, et al. Assay variation confounds the diagnosis of hypovitaminosis D: a call for standardization. J Clin Endocrinol Metab 2004;89:3152–7.
- 48. Carter GD, Carter R, Jones J, Berry J. How accurate are assays for 25-hydroxyvitamin D? Data from the international vitamin D external quality assessment scheme. Clin Chem 2004;50:2195–7.
- Thomas JB, Kline MC, Gill LM, et al. Preparation and value assignment of standard reference material 968c fat-soluble vitamins, carotenoids, and cholesterol in human serum. Clin Chim Acta 2001;305:141–55.
- Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006; 84:18–28.
- 51. Cranney A, Horsley T, O'Donnell S, et al. Effectiveness and safety of vitamin D in relation to bone health. Evidence report/technology assessment no. 158. Prepared by the University of Ottawa Evidence-based Practice Center (UO-EPC) under contract no. 290-02-0021. AHRQ publication no. 07-E013. Rockville, MD: Agency for Healthcare Research and Quality, August 2007;Internet: http://www.ahrq.gov/downloads/ pub/evidence/pdf/vitamind/vitad.pdf (accessed 7 November 2007).
- Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr 2000;72:690–3.

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