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Trends in Use of High Dose Vitamin D Supplements Exceeding 1,000 or 4,000 International Units Daily, 1999-2014

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Introduction

Since 2000 there has been a surge in research on possible health benefits of vitamin D. However, a 2011 Institute of Medicine Report concluded that vitamin D was beneficial for bone health but evidence was insufficient for extra-skeletal health.[1] Several large-scale trials are ongoing to evaluate the effect of vitamin D supplementation on extra-skeletal outcomes.[2] The IOM report noted possible harm (e.g. hypercalcemia, soft tissue or vascular calcification) for intakes above the tolerable upper limit, which is the highest level of intake likely to pose no risk of adverse effects for most adults.[1]

The recommended dietary allowance for vitamin D is 600 IU/day for adults aged ≤70 years and 800 IU/day for those >70. The tolerable upper limit is 4,000 IU/day; beyond this level risk of toxic effects increases.[1] Multivitamins typically contain about 400 IU/day; consumption ≥1,000 IU/day likely indicates intentionally seeking supplemental vitamin D.

We sought to capture trends in supplemental vitamin D intake ≥1,000 and ≥4,000 IU/day between 1999 and 2014.

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institutes of Health or the US Department of Health and Human Services.

Author Contributions: MRR and RO had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept: PLL
Design: PLL, LH, MRR, EDM, CS
Acquisition, analysis, or interpretation of data: MRR, RO
Drafting of the manuscript: MRR, PLL
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Methods

Repeat cross-sectional data from the nationally representative National Health and Nutrition Examination Survey (NHANES) were used. NHANES, which includes survey and examination components, samples non-institutionalized U.S. residents through a complex, stratified, multi-stage probability sampling design with certain populations over-represented (overall response = 74%).[5] Informed consent was obtained; the National Center Health Statistics Research Ethics Review Board approves the protocol annually.

For this analysis, we excluded participants who were aged <20 years, pregnant, or had inadequate supplement information. Participants self-reported supplemental vitamin D daily intake for the past 30 days; they were asked to bring supplement bottles to aid in reporting.[5]

STATA version 14.1 was used (StataCorp LP). Sample weights were applied. The prevalence of vitamin D supplementation ≥1,000 and ≥4,000 IU/day was calculated for each survey period overall and by sex, age and race/ethnicity. Linear trends were tested via linear regression; statistical significance was defined by two-sided p-values <0.05.

Results

The 39,243 participants were, in weighted analyses, mean±SD 46.6±16.8 years old, 51.1% women and 69.7% non-Hispanic white. The prevalence of supplemental vitamin D use ≥1,000 IU/day in 2013-14 was 18.2% (95% CI: 16.0-20.7%), which was higher than in 1999-2000 [0.3% (0.1-0.5%)]; p-trend <0.001 (Table 1).

In 2013-14, prevalence of supplemental intake ≥4,000 IU/day was 3.2% (2.5-4.0%) (Table 2). Prior to 2005-06, prevalence of intake ≥4,000 IU/day was <0.1% (p-trend 2007-08 to 2013-14: <0.001).

Trends of increasing supplemental vitamin D use were found for most age groups, race/ethnicities, and both sexes; though there were interactions (see tables). In 2013-14, intake ≥4,000 IU/day was highest in women [4.0% (2.9-5.5%)], Non-Hispanic whites [3.9% (3.0-5.1%)], and those aged ≥70 [6.6% (4.2-10.2%)].

Discussion

From 1999 to 2014 the number of U.S. adults taking vitamin D supplements ≥1,000 and ≥4,000 IU/day has increased. Overall, 3% of the population exceeded the tolerable upper limit of 4,000 IU/day, and some may be experiencing adverse effects as a consequence. Consumption ≥1,000 IU/day may not lead to harm, but likely indicates intentionally seeking supplemental vitamin D. These findings extend a prior NHANES report documenting an increase in vitamin D supplement intake ≥600 IU/day, particularly among women, non-Hispanic whites, and older persons, from 1988-2010.[6] 25(OH)D concentrations have also modestly increased over this time-frame.[6] One limitation of our study is that data were self-reported; however, participants were asked to bring supplement bottles to aid in reporting.

While research has emphasized possible benefits of vitamin D, high dosages pose potential risks.[1] A randomized clinical trial with high dose vitamin D supplementation found increased risk of fractures and falls,[3] and increased risk of kidney stones has been found with vitamin D taken in combination with calcium.[4] Some epidemiologic investigations have reported adverse associations of high 25(OH)D with prostate cancer, pancreatic cancer and all-cause mortality.[1]

Characterizing trends in vitamin D supplementation – particularly at doses above the tolerable upper limit– has important and complex public health and clinical implications. Meanwhile, potential benefits, or even harms, of high dosage vitamin D supplementation are unknown.

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Table 1

Trends in the prevalence (95% CI) of vitamin D supplement use ≥1,000 IU per day, overall and stratified by sex, racial/ethnic and age groups: NHANES 1999-2014[a,b]

	1999-2000 N=4,580	2001-02 N=5,080	2003-04 N=4,796	2005-06 N=4,636	2007-08 N=5,043	2009-10 N=5,401	2011-12 N=4,794	2013-14 N=4,913	p-trend[c,d]
Overall	0.3 (0.1-0.5)	0.2 (0.1-0.4)	0.4 (0.3-0.8)	0.7 (0.5-1.2)	4.4 (3.7-5.1)	9.4 (8.2-10.8)	15.8 (13.5-18.4)	18.2 (16.0-20.7)	<0.001
Sex									
Women	0.4 (0.2-1.0)	0.3 (0.1-0.6)	0.7 (0.4-1.2)	1.1 (0.6-1.9)	6.7 (5.7-7.9)	12.9 (11.1-15.1)	20.9 (17.6-24.6)	25.9 (22.8-29.3)	<0.001
Men	0.1 (0.0-0.5)	0.1 (0.0-0.2)	0.2 (0.1-0.4)	0.4 (0.2-0.8)	2.0 (1.5-2.7)	5.7 (4.6-7.0)	10.3 (8.5-12.5)	10.3 (8.7-12.3)	<0.001
Race/Ethnicity[e]									
Non-Hispanic Whites	0.3 (0.2-0.7)	0.2 (0.1-0.5)	0.6 (0.3-1.1)	0.9 (0.5-1.5)	5.9 (4.9-7.0)	11.9 (10.7-13.3)	19.3 (16.1-23.0)	21.8 (19.3-24.6)	<0.001
Non-Hispanic Blacks	0.2 (0.0-1.1)	0.1 (0.0-0.8)	0.2 (0.0-0.8)	0.4 (0.1-0.8)	1.4 (0.8-2.4)	5.8 (4.2-8.1)	9.5 (7.0-12.7)	11.7 (9.5-14.4)	<0.001
Hispanics	0	0	0	0	1.2 (0.7-1.9)	4.4 (3.1-6.4)	7.8 (5.7-10.5)	10.0 (6.7-14.8)	n/a
Mexican Americans	0.1 (0.0-0.3)	0.4 (0.1-1.2)	0.1 (0.1-0.3)	0.0 (0.0-0.2)	0.4 (0.2-0.7)	2.2 (1.5-3.2)	4.2 (2.8-6.4)	8.1 (6.0-10.9)	<0.001
Asian Americans[f]	n/a	n/a	n/a	n/a	n/a	n/a	11.4 (9.1-14.3)	16.8 (13.5-20.7)	n/a
Age									
20-39y	0	0.0 (0.0-0.2)	0	0.2 (0.1-0.6)	1.2 (0.7-2.2)	3.1 (2.2-4.3)	7.2 (5.4-9.5)	8.0 (6.8-9.4)	n/a
40-59y	0.2 (0.1-1.1)	0.2 (0.1-0.8)	0.3 (0.1-1.3)	0.9 (0.5-1.8)	4.3 (3.5-5.1)	9.3 (7.3-11.8)	14.2 (11.2-17.7)	16.8 (14.0-20.0)	<0.001
60-69y	1.2 (0.4-3.2)	0.0 (0.0-0.2)	1.6 (1.1-2.3)	1.3 (0.6-2.7)	11.3 (8.5-14.8)	17.8 (14.0-22.2)	27.8 (20.9-35.9)	30.9 (24.8-37.7)	<0.001
≥70y	0.4 (0.1-2.2)	0.6 (0.2-1.6)	1.1 (0.5-2.5)	1.5 (1.1-2.0)	8.6 (5.6-13.1)	21.2 (18.3-24.4)	32.8 (26.7-39.7)	38.5 (31.8-45.7)	<0.001

[a] Estimates weighted to be nationally representative.

[b] '0' Corresponds to cells with no observations during survey period; '0.0' corresponds to proportion less than 0.01.

[c] Linear trend tested via linear regression by modeling survey period as a continuous variable. Trend tests were not applicable (n/a) when intake was '0' in any survey period.

[d] Trends significantly different (p for interaction <0.001) by race, sex, and age categories.

[e] Individuals self-identified their race and whether they were of Hispanic ethnicity. Those who reported other race – including multi-racial – are reported in the total population but not separately.

[f] Not applicable (n/a): Oversampling and inclusion of the racial/ethnic group response "Non-Hispanic Asians" began in the 2011-12 cycle.

Table 2

Trends in the prevalence (95% CI) of vitamin D supplement use ≥4,000 IU per day overall and stratified by sex, racial/ethnic and age groups: NHANES 2007-2014[a,b,c]

	2007-08 N=5,043	2009-10 N=5,401	2011-12 N=4,794	2013-14 N=4,913	p-trend [d,e]
Overall	0.2 (0.1-0.4)	0.8 (0.5-1.2)	1.8 (1.1-3.0)	3.2 (2.5-4.0)	<0.001
Sex					
Women	0.2 (0.1-0.7)	0.9 (0.5-1.4)	2.2 (1.2-4.0)	4.2 (3.0-5.7)	<0.001
Men	0.1 (0.0-0.6)	0.6 (0.3-1.4)	1.4 (0.9-2.2)	2.2 (1.6-3.0)	<0.001
Race/Ethnicity [f]					
Non-Hispanic Whites	0.2 (0.1-0.6)	1.1 (0.7-1.6)	2.3 (1.3-4.1)	3.9 (3.0-5.1)	<0.001
Non-Hispanic Blacks	0.3 (0.1-0.9)	0.4 (0.1-1.2)	0.8 (0.4-1.4)	2.0 (1.4-2.9)	<0.001
Hispanics	0	0.1 (0.0-0.6)	1.0 (0.4-2.6)	1.8 (0.8-3.8)	n/a
Mexican Americans	0	0.0 (0.0-0.3)	0.3 (0.1-1.5)	0.5 (0.2-1.5)	n/a
Asian Americans [g]	n/a	n/a	1.8 (1.1-3.1)	3.3 (2.3-4.8)	n/a
Age					
20-39y	0	0.2 (0.0-1.0)	0.9 (0.5-1.7)	1.6 (1.0-2.5)	n/a
40-59y	0.3 (0.1-0.9)	0.9 (0.4-1.9)	2.1 (0.8-5.6)	2.2 (1.9-2.7)	<0.001
60-69y	0.6 (0.1-2.7)	1.6 (0.9-2.9)	1.9 (1.0-3.9)	6.6 (4.8-9.1)	<0.001
≥70y	0	1.3 (0.6-2.7)	3.5 (1.9-6.4)	6.6 (4.2-10.2)	n/a

[a] Estimates weighted to be nationally representative.

[b] '0' Corresponds to cells with no observations during survey period; '0.0' corresponds to proportion less than 0.01.

[c] Survey periods between 1999-2006 had proportion less than 0.1 overall and across all demographic groups.

[d] Linear trend tested via linear regression by modeling survey period as a continuous variable. Trend tests were not applicable (n/a) when intake was '0' in any survey period.

[e] Trends significantly different by race (i.e. black vs. white; p for interaction 0.01) and age categories (p for interaction <0.001).

[f] Individuals self-identified their race and whether they were of Hispanic ethnicity. Those who reported other race – including multi-racial – are reported in the total population but not separately.

[g] Not applicable (n/a): Oversampling and inclusion of the racial/ethnic group response "Non-Hispanic Asians" began in the 2011-12 cycle.