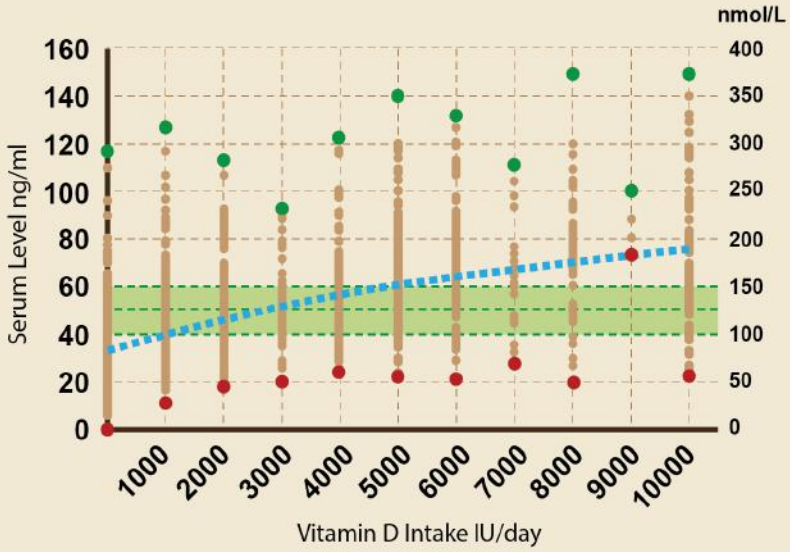
Serum Level vs Intake



Garland, C.F., French, C.B., Baggerly, Leo L., Heaney, Rorbert P., (2011) Vitamin D Supplement Doses and Serum 25-Hydroxyvitamin D in the Range Associated with Cancer Prevention. ANTICANCER RESEARCH 31: 617-622.

Moving Research into Practice

Vitamin D

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Moving Research into Practice

May 2016

Scientists' Call to D*action

The Vitamin D Deficiency Epidemic

40-75% of the world's population is vitamin D deficient.

The causal link between severe vitamin D deficiency and rickets or the bone disease of osteomalacia is overwhelming, while the link between vitamin D insuffiency and osteoporosis with associated decreased muscle strength and increased risk of falls in osteoporotic humans is well documented by evidence-based intervention studies.

There are newly appreciated associations between vitamin D insufficiency and many other diseases, including tuberculosis, psoriasis, multiple sclerosis, inflammatory bowel disease, type-1 diabetes, high blood pressure, increased heart failure, myopathy, breast and other cancers which are believed to be linked to the non-calcemic actions of the parent vitamin D and its daughter steroid hormone.

Based on the evidence we now have at hand, action is urgent.

It is projected that the incidence of many of these diseases could be reduced by 20%-50% or more, if the occurrence of vitamin D deficiency and insufficiency were eradicated by increasing vitamin D intakes through increased UVB exposure, fortified foods or supplements. The appropriate intake of vitamin D required to effect a significant disease reduction depends on the individual's age, race, lifestyle, and latitude of residence. The latest Institute of Medicine (IOM) report, 2010, indicates 10,000 IU/day is considered the NOAEL (no observed adverse effect level). 4000 IU/day can be considered a safe upper intake level for adults aged 19 and older.

It is well documented that the darker the skin, the greater the probability of a vitamin D deficiency. Even in southern climates, 55% of African Americans and 22% of Caucasians are deficient.

More than 1 billion people worldwide are affected at a tremendous cost to society.

A Scientists' Call to Action has been issued to alert the public to the importance to have **vitamin D serum levels between 40 and 60 nanograms/milliliter (100-150 nanomoles/liter)** to prevent these diseases. Implementing this level is safe and inexpensive.

The benefit of an adequate vitamin D level to each individual will be better overall health and a reduction in illnesses and, ultimately, a significant reduction in health care costs. The benefit of adequate vitamin D levels to society/businesses is a more productive workforce and, lower health care costs.

The D*action project has as its purpose to serve as a model for public health action on vitamin D. It is a test bed for techniques, and for providing outcome evaluation at a community level.

Revised 10/16/15

315 S. Coast Hwy 101, U-87, Encinitas, CA 92024
www.grassrootshealth.net

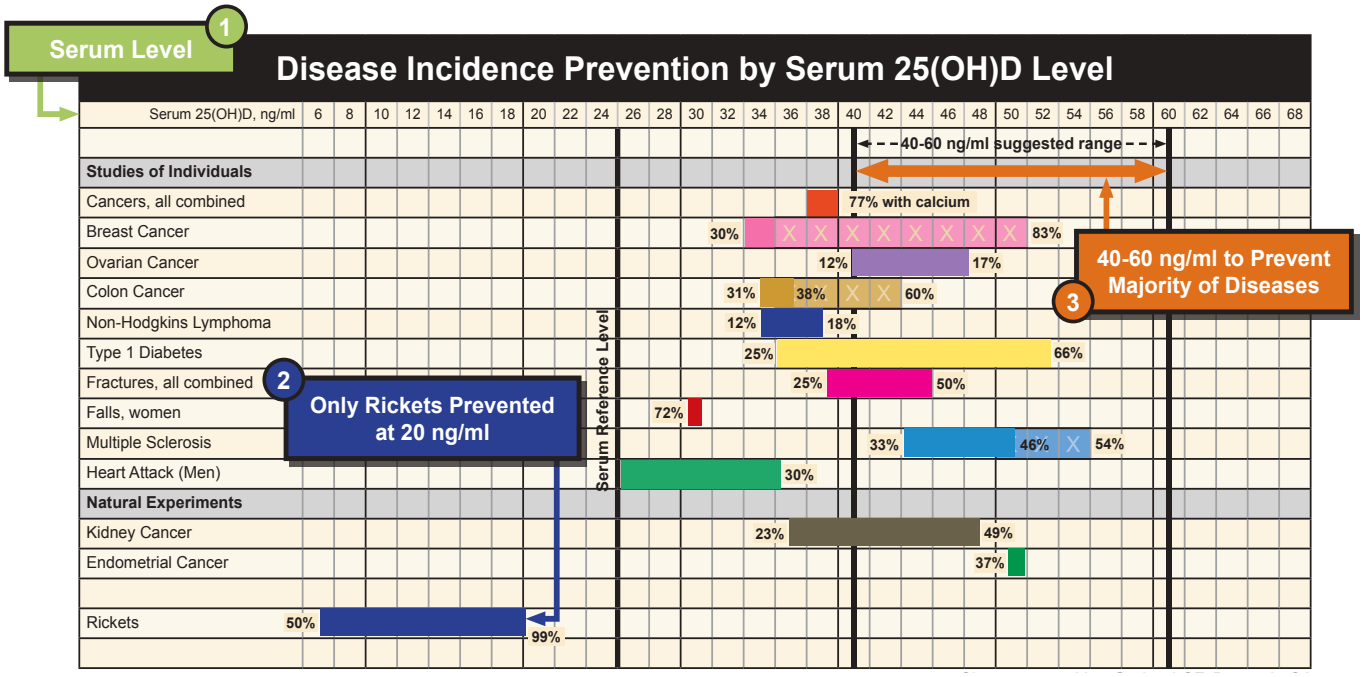
Dosing

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Disease Incidence Prevention by Serum 25(OH)D Level

Select Clinical Trials and Epidemiological Studies



Results from multiple studies regarding the association between 25(OH)D and various diseases were summarized according to a common reference level of 25 ng/ml, the average concentration in the US population.

The percent reductions represent what can be expected in the general population if concentrations were raised to the concentrations specified on the chart.

There were significant reductions in disease risk with increasing 25(OH)D concentrations, especially at 40 ng/ml and above.

Chart Date: 3/23/10

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Serum Level vs Intake (Ages 18+ years)

GrassrootsHealth D*action Cohort (N=7,324)

In an analysis of vitamin D serum levels and daily supplemental vitamin D intake amounts for 7,324 D*action participants, we found that while average serum level rises with increased intake, there is a wide range of individual serum levels at any given intake amount.

For example, with a supplemental intake of 4000 IU/day, serum levels were observed from 20 ng/ml (50 nmol/L) to 120 ng/ml (300 nmol/L).

The GrassrootsHealth Scientists Panel of 48 expert vitamin D researchers and medical practitioners hold the position that the serum level should be between 40-60 ng/ml (100-150 nmol/L).

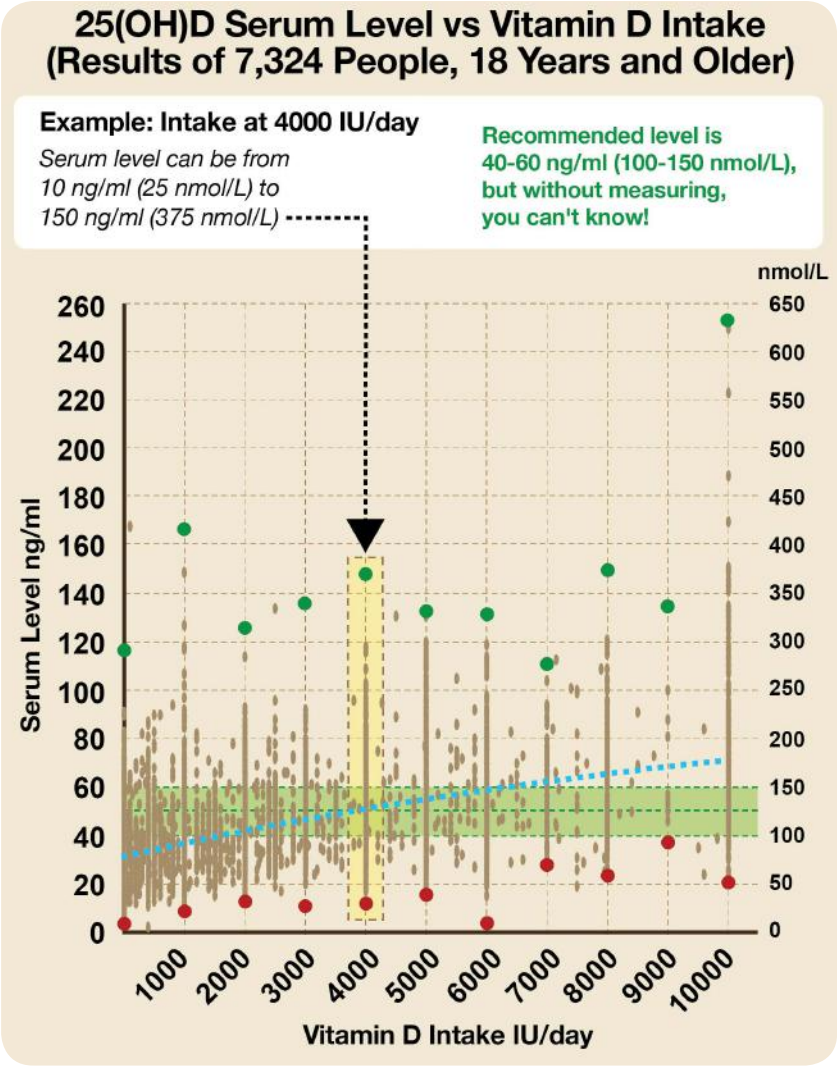
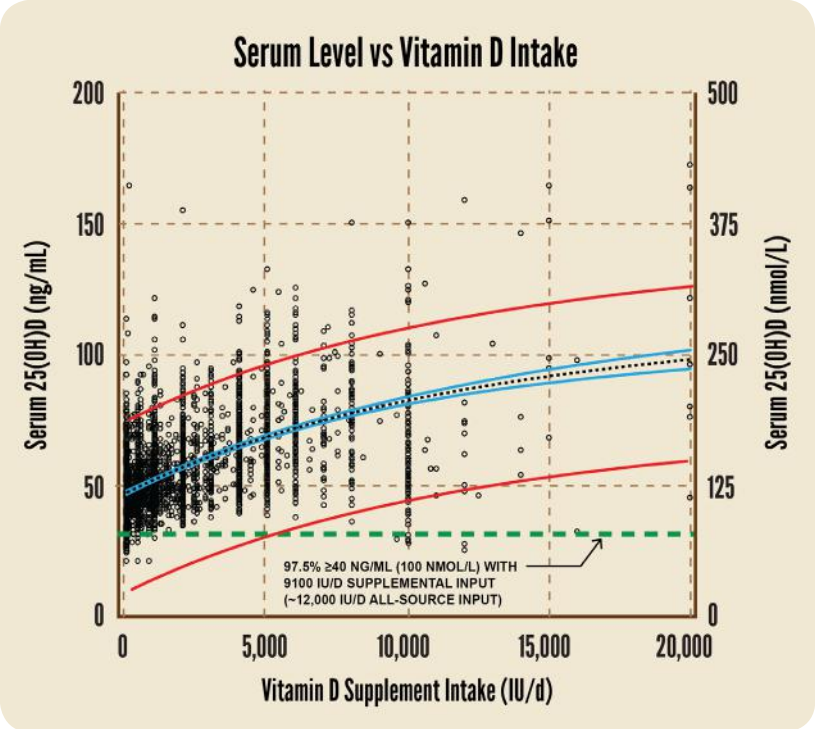


Chart Date: 12/9/15

 Garland, C.F., French, C.B., Baggerly, Leo L., Heaney, Rorbert P., (2011) Vitamin D Supplement Doses and Serum 25-Hydroxyvitamin D in the Range Associated with Cancer Prevention. ANTICANCER RESEARCH 31: 617-622.

Serum 25(OH)D vs Vitamin D Supplement Intake

GrassrootsHealth D*action Cohort (N=3,657)



This figure shows a plot of the 25(OH)D values as a function of reported vitamin D intake amounts.

The black dotted line is the best fit line through the data, the blue lines are the 95% confidence limits, and the outer red lines are the 95% probability bands.

The point at which the horizontal green line at 40 ng/ml intersects with the lower probability band (red line) reflects the supplemental input necessary to ensure that 97.5% of the cohort would have a 25(OH)D concentration ≥40 ng/ml (~9100 IU/day).

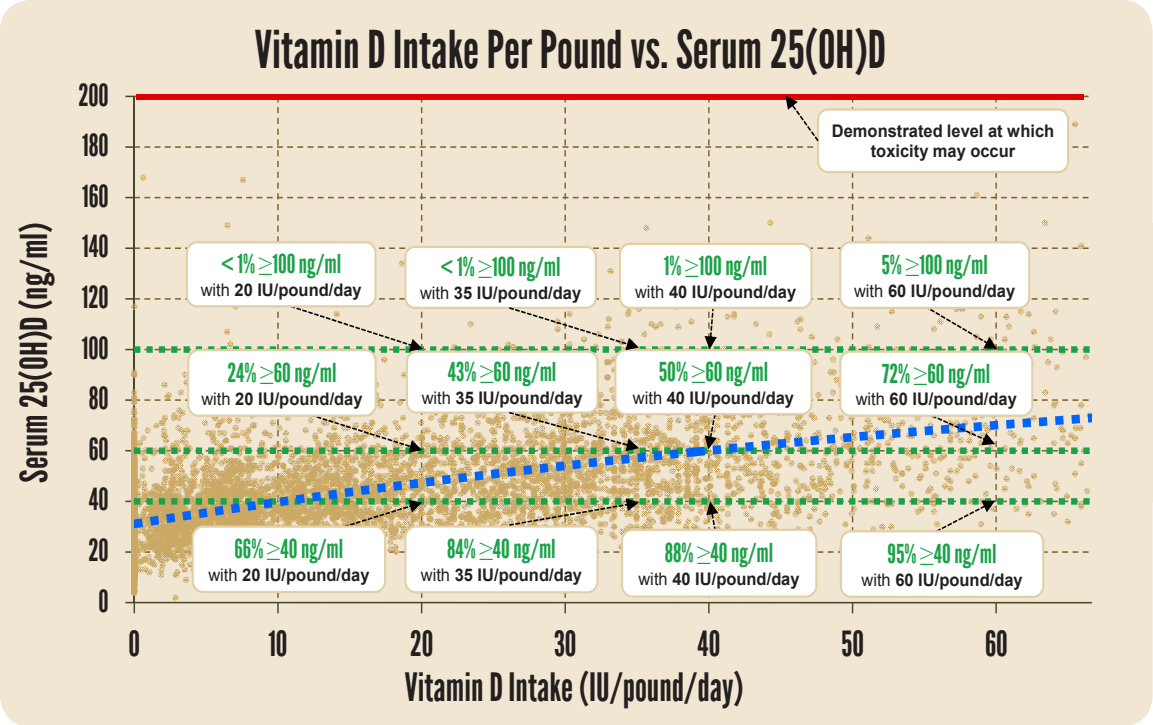
The best fit line intersects the Y-axis at a value of 34 ng/ml, reflecting an intake from food and sun amounting to ~3000 IU/day. Therefore, the total intake required to achieve 40 ng/ml in 97.5% is ~12000 IU/day.

This figure demonstrates: (i) the gradual rise of serum 25(OH)D with increasing dosage; (ii) there is a very large spread of 25(OH)D values at each dose; and (iii) very few individuals had serum 25(OH)D values above 200 ng/ml.

Chart Date: 2/2/15

Vitamin D Supplement Intake Per Pound vs. Serum 25(OH)D Concentration (Ages 18+ Years)

GrassrootsHealth D*action Cohort (N= 7,324)



This figure shows a plot of the 25(OH)D values as a function of reported vitamin D intake amounts per pound. The blue dotted line is the best fit line through the data.

Shown on the figure are the percent of participants who are at or above 40, 60, and 100 ng/ml for various vitamin D supplement intake amounts.

1% or less of participants have serum levels ≥100 ng/ml with 40 IU/pound/day or less.

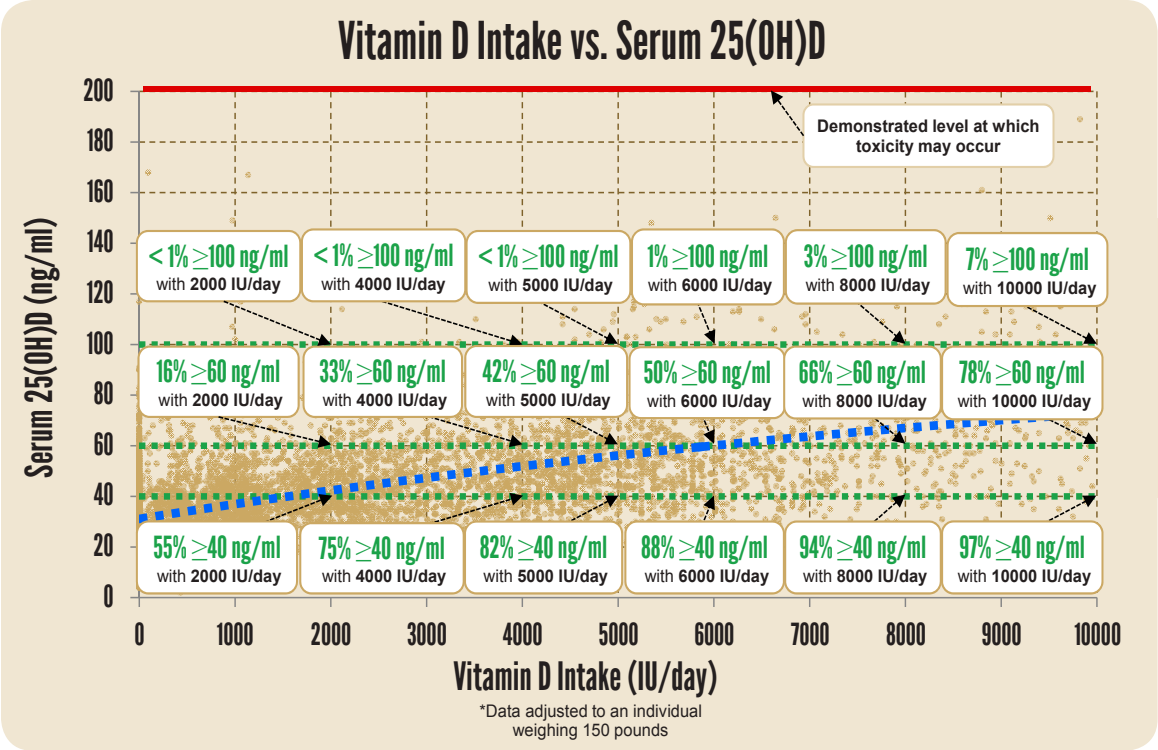
Chart Date: 12/1/15

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Vitamin D Supplement Intake vs. Serum 25(OH)D Concentration (Ages 18+ Years)

GrassrootsHealth D*action Cohort (N= 7,324)



This figure shows a plot of the 25(OH)D values as a function of reported vitamin D intake amounts, adjusted to an individual weighing 150 pounds. The dotted blue line is the best fit line through the data.

Shown on the figure are the percent of participants who are at or above 40, 60, and 100 ng/ml for various vitamin D supplement intake amounts.

1% or less of participants have serum levels ≥100 ng/ml with 6000 IU/day or less.

Chart Date: 12/1/15

Vitamin D Dose (IU) to Ensure 90% of Adults Achieve Specified 25(OH) D Concentration (Ages 18+ years)*

GrassrootsHealth D*action Cohort (N=7,324)

Vitamin D intake observed to produce noted 25(OH)D serum levels in 90% of adults (age 18 years and older), weighing 150 lbs. (N=7324)

RECOMMENDED RANGE: 40-60 ng/ml

WHAT TO DO

1. **Test**
2. **Establish recommended intake level**
3. **Test again in 3-6 months**

(For supplements, vitamin D3, cholecalciferol may be used.)

Individuals should consult with a health care practitioner to develop a custom plan.

Change in Serum Level Based on Intake (IU/day) for 90% of Adults* (N=7324)

Current Level (ng/ml) \ Expected Level (ng/ml)	20	30	40	50	60
10	2000	4000	6000	10,000	10,000
15	1000	3000	6000	9000	10,000
20		2000	5000	8000	10,000
25		1000	4000	7000	10,000
30			3000	6000	10,000
35			1000	5000	9000
40				3000	8000
45				2000	6000
50					4000

** values rounded to the nearest 1000 IU; highest recommended intake is 10,000 IU/day*

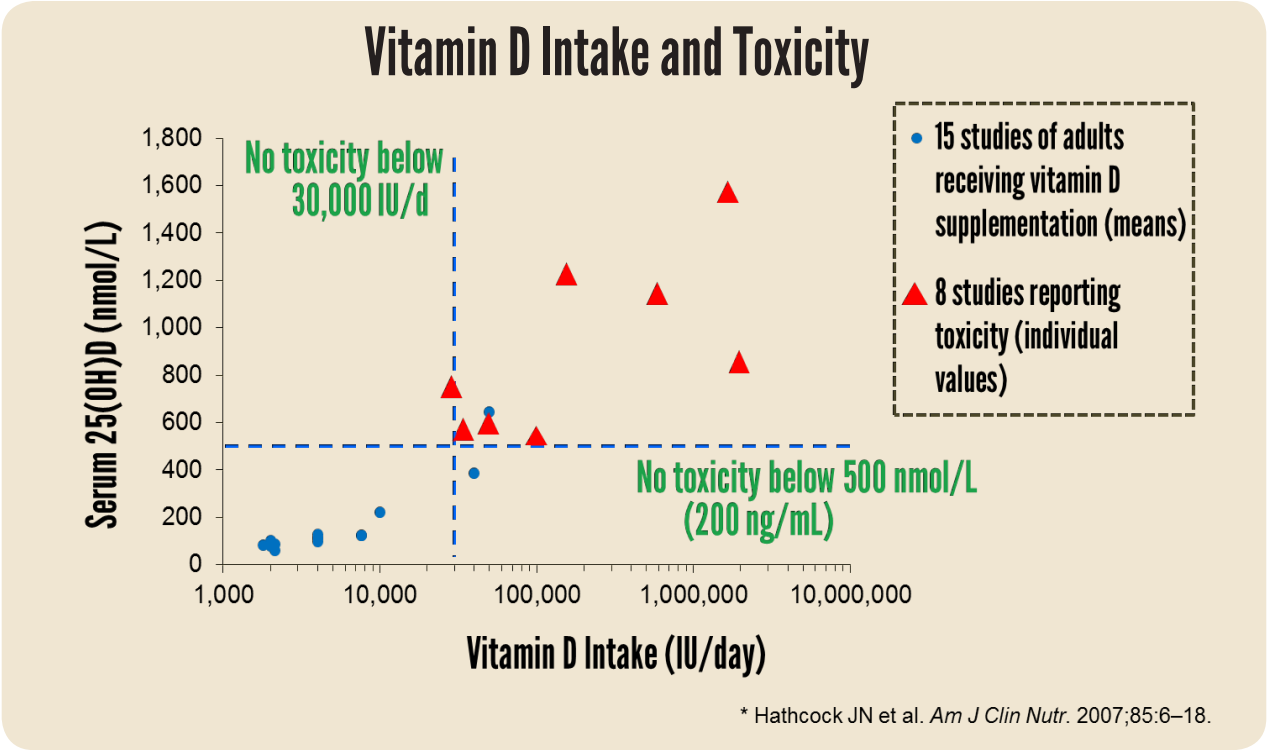
Example: With a starting serum level of 20 ng/ml, an additional intake of approximately 5000 IU/day would be sufficient for 90% of adults (age 18 years and older, weighing 150 lbs) to achieve a serum level of at least 40 ng/ml.

Based on a plot of 25(OH)D values as a function of reported vitamin D intake amounts, the doses in this chart indicate the supplemental input (IU) necessary to ensure that 90% of the population would achieve the specified serum level increase (for an individual weighing 150 lbs, 68 kg).

Chart Date: 12/9/15

Vitamin D Intake and Toxicity

Vitamin D Clinical Trials (N=15) and Case Studies (N=8)



* Hathcock JN et al. *Am J Clin Nutr.* 2007;85:6–18.

This meta-analysis found no toxicity below an intake amount of 30,000 IU/day and below a serum concentration of 200 ng/ml.

There is a significant margin of safety for the recommended concentration range of 40-60 ng/ml.

Chart Date: January 2007. (seminar on 12/2014)

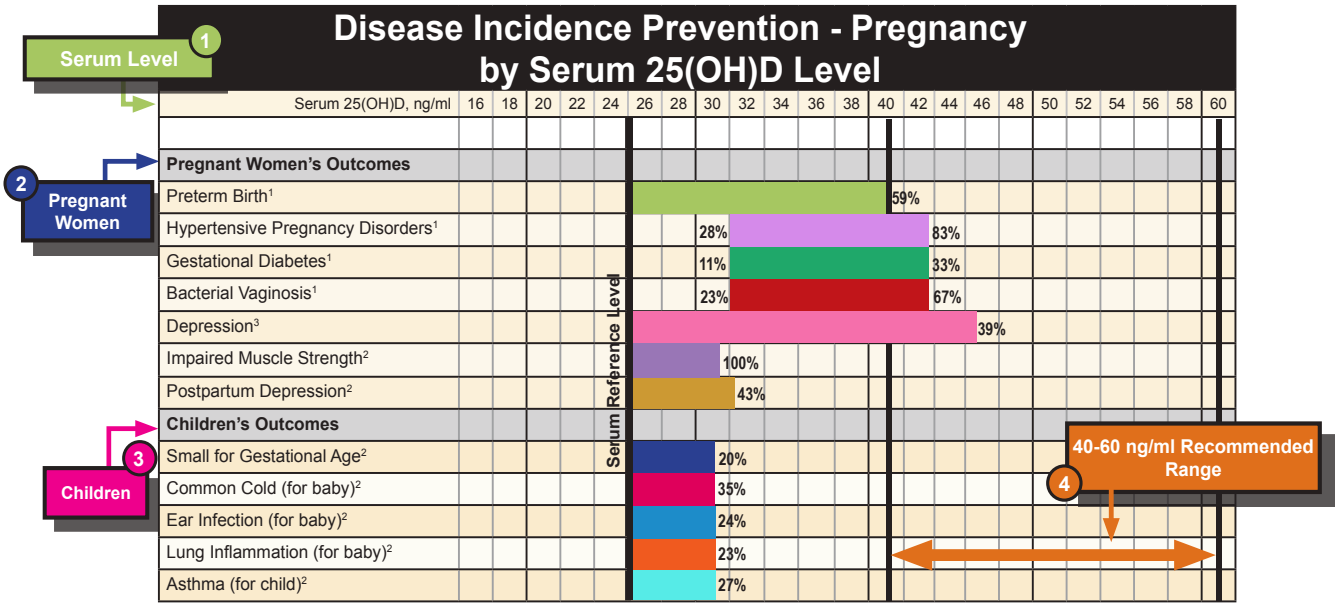
Pregnancy

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Disease Incidence Prevention for Pregnancy Complications and Birth Outcomes

Select Clinical Trials and Epidemiological Studies



Results from multiple studies regarding the association between 25(OH)D and pregnancy complications and birth outcomes were summarized according to a common reference level of 25 ng/ml, the average concentration in the US population.

The percent reductions represent what can be expected in the general population if concentrations were raised to the concentrations specified on the chart from 25 ng/ml.

There were significant reductions in adverse clinical outcomes related to pregnancy and childhood with increasing maternal 25(OH)D concentrations, especially at 40 ng/ml and above.

Chart Date: 2/1/15

Fitted LOESS Curve of 25(OH)D Concentration within 6 Weeks of Delivery by Gestational Age (Weeks) at Birth

NICHD & TRF Combined Cohort (N=509)

Using data from two supplementation trials conducted in South Carolina (NICHD and TRF), a plot of gestation week at birth as a function of 25(OH)D concentration with a fitted LOESS curve was constructed.

This figure shows a zoom on the fitted LOESS curve with confidence bounds showing gestational age at birth initially rising steadily with increasing 25(OH)D concentration and then plateauing at approximately 40 ng/ml.

After adjusting for race/ethnicity, maternal age, and insurance status, participants with 25(OH)D concentrations ≥40 ng/ml had a 59% lower risk of preterm birth than participants with concentrations ≤20 ng/ml.

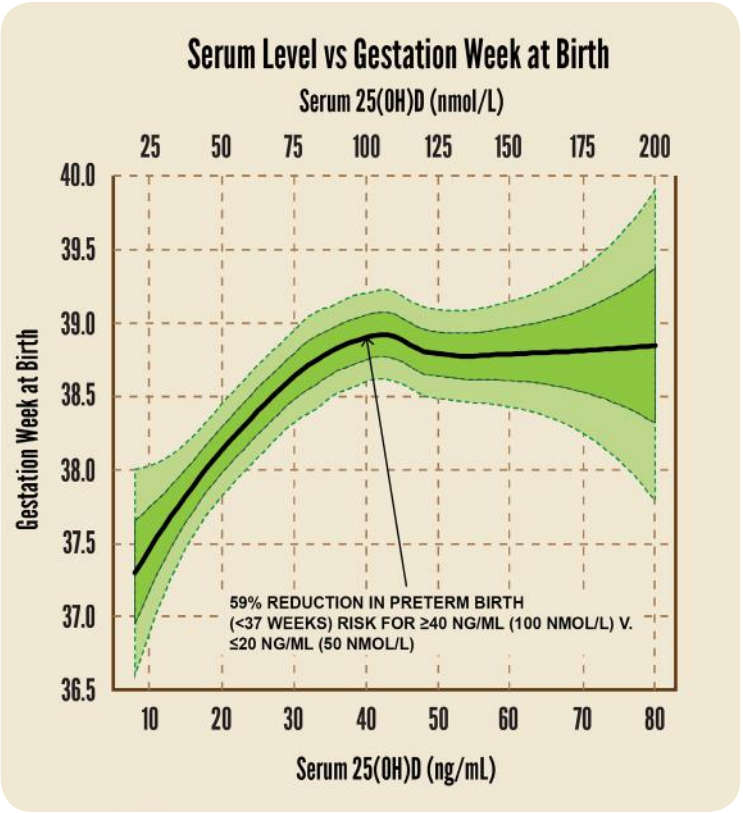


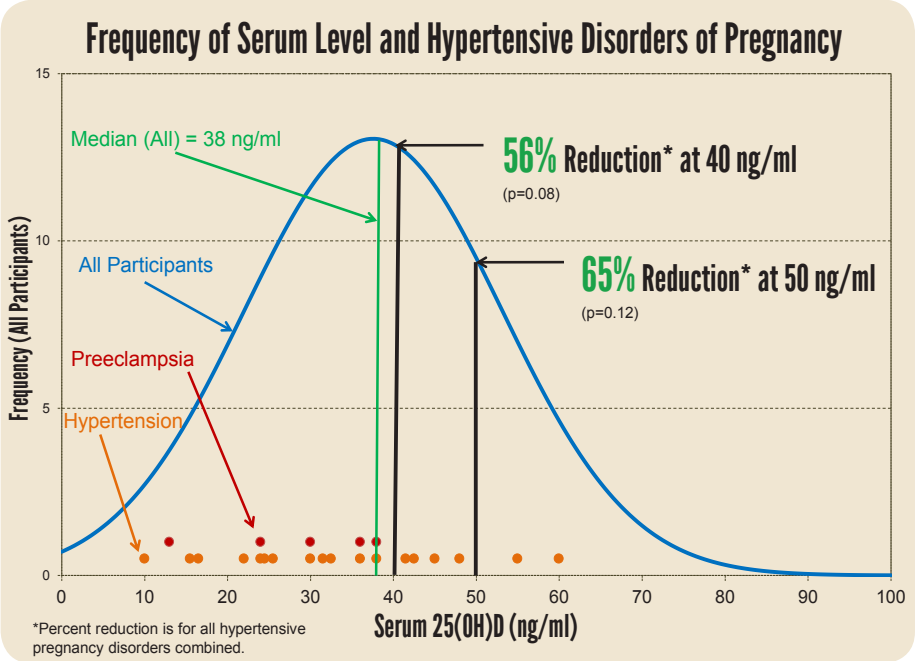
Chart Date: 11/11/15

 Wagner et al. Post-hoc analysis of vitamin D status and reduced risk of preterm birth in two vitamin D pregnancy cohorts compared with South Carolina March of Dimes 2009-2011 rates. J Steroid Biochem Mol Biol, 2016. Jan;155(Pt B):245-51.

Frequency Distribution of 25(OH)D Concentration and Hypertensive Disorders of Pregnancy within 6 Weeks of Delivery

Pooled NICHD and TRF Trial (N=505)

The occurrence of hypertensive disorders of pregnancy were calculated according to achieved 25(OH)D concentration using data from two supplementation trials conducted in South Carolina (NICHD and TRF).



The median achieved 25(OH)D concentration within 6 weeks of delivery was 38 ng/ml.

Among the 22 participants diagnosed with a hypertensive disorder, 16 (73%) had achieved 25(OH)D concentrations below 40 ng/ml. All preeclampsia cases had concentrations <40 ng/ml.

Women with achieved 25(OH)D concentrations ≥40 ng/ml had a 56% lower risk of hypertensive pregnancy disorders than women with concentrations <40 ng/ml (P=0.08). Those who achieved 50 ng/ml had a 65% lower risk compared to those who did not (P=0.12).

Achieving a 25(OH)D concentration of ≥40 ng/ml reduced the risk of hypertensive pregnancy disorders in this study.

Chart Date: 10/8/15

Serum 25(OH)D Concentration by Race/Ethnicity (U.S. Women Aged 18-45 Years)

2005-2006 NHANES (N=1,479)

Among U.S. women of child-bearing age, only 7% have 25(OH)D concentrations at or above 40 ng/ml.

A majority of Black women (79%) and Hispanic women (59%) have concentrations below 20 ng/ml.

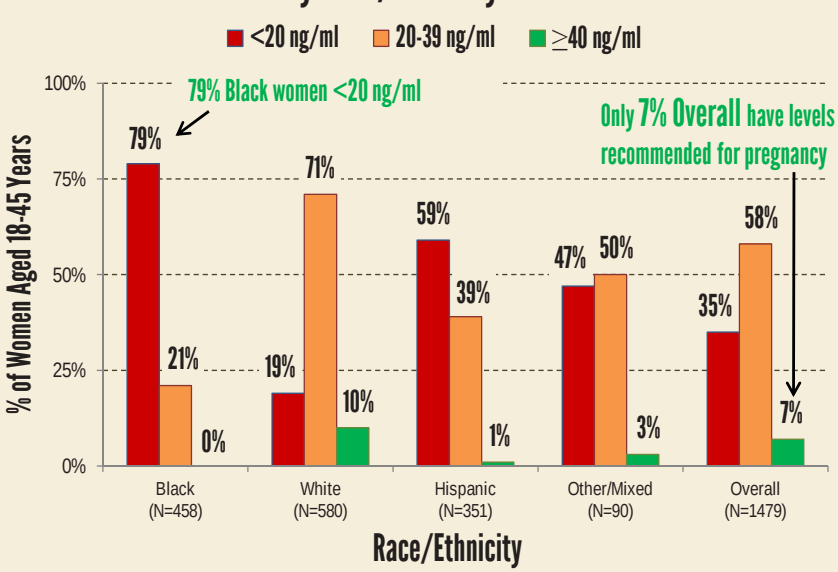
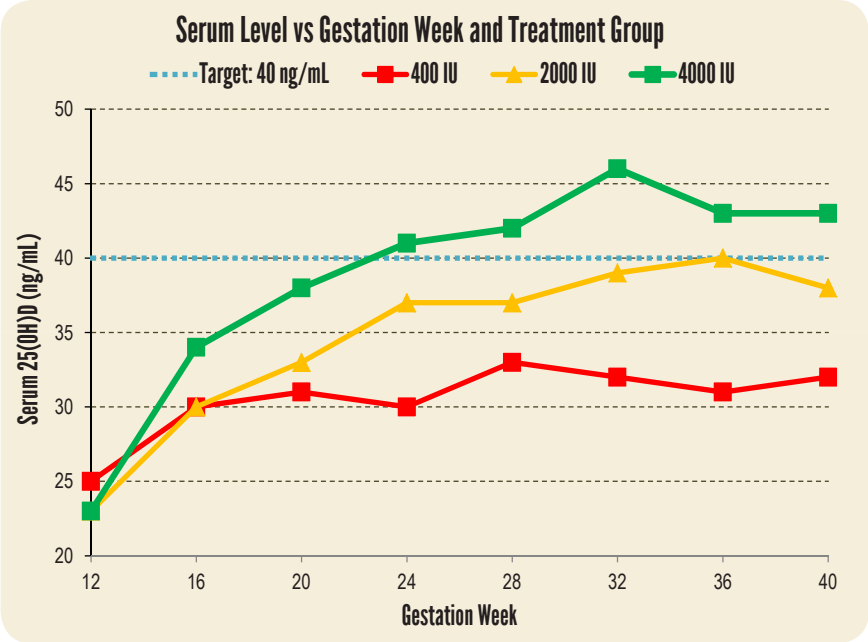


Chart Date: 6/26/15

Average Serum 25(OH)D Concentration by Gestation Week and Treatment Group

NICHD & TRF (N=509)

Using data from two supplementation trials conducted in South Carolina (NICHD and TRF), mean 25(OH)D concentrations were plotted by gestation week for the three vitamin D treatment groups: 400 IU/day, 2000 IU/day, and 4000 IU/day.



Average serum levels rose more quickly for the 4000 IU/day treatment group and ≥40 ng/ml was achieved within ~10 weeks.

Average serum levels did not reach and maintain ≥40 ng/ml for the 400 or 2000 IU/day treatment groups.

Chart Date: 9/2/15

Cancer

GrassrootsHealth
Moving Research into Practice

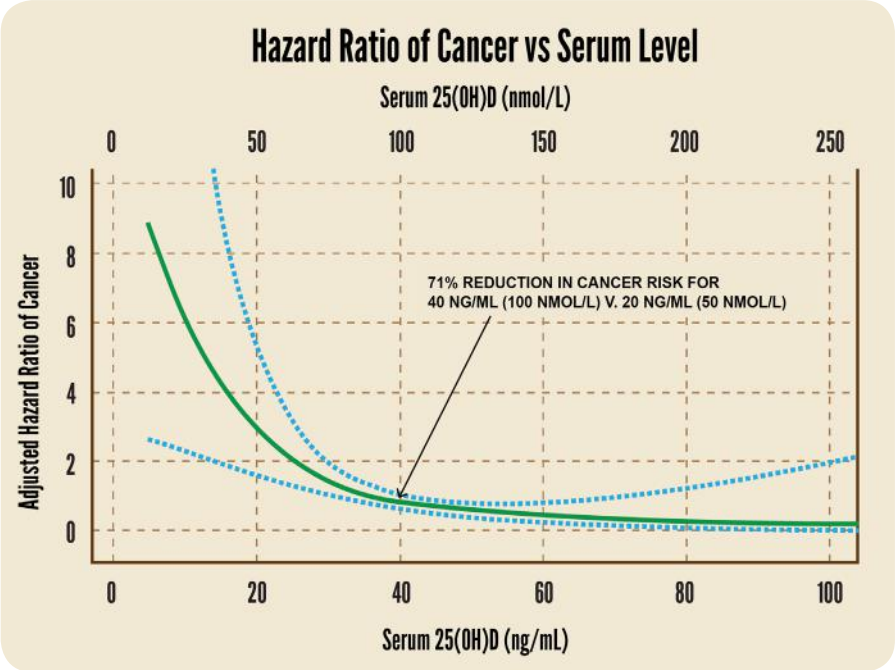
www.grassrootshealth.net

Cancer Incidence is 71% Lower for ≥40 ng/ml vs <20 ng/ml (Women Ages 55+ Years)

Pooled GrassrootsHealth and Lappe Cohort (N=2304)

Data from two cohorts of women aged 55+ years were pooled: the GrassrootsHealth cohort (N=1,135) and the Lappe cohort from a randomized clinical trial (N=1,169).

The median 25(OH)D was 48 ng/ml in the GrassrootsHealth cohort and 30 ng/ml in the Lappe cohort, affording a broad range of 25(OH)D concentrations.



The non-linear association between serum 25(OH)D and cancer risk (figure) shows the greatest decrease in risk occurred between ~10-40 ng/ml (reduction in risk from 20 ng/ml to 40 ng/ml was ~70%).

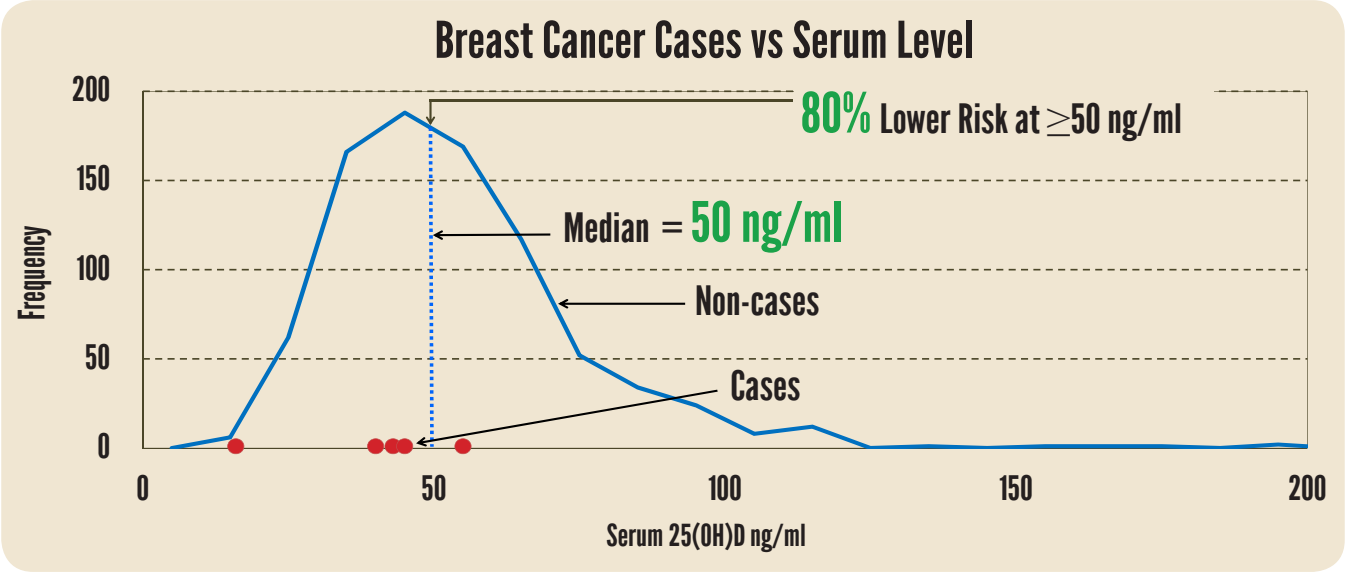
These findings suggest that increasing 25(OH)D concentrations to a minimum of 40 ng/ml could substantially reduce cancer incidence and associated mortality in the population.

Chart Date: 11/4/15

 McDonnell SL, Baggerly C, French CB, Baggerly LL, Garland CF, Gorham ED, Lappe JM, Heaney RP. Serum 25-Hydroxyvitamin D Concentrations ≥40 ng/ml are Associated with >65% Lower Cancer Risk: Pooled Analysis of Randomized Trial and Prospective Cohort Study. PLoS One. 2016

Frequency Distribution of 25(OH)D among Cases and Non-Cases of Breast Cancer (Women Aged 60+ Years)

GrassrootsHealth D*action Cohort (N=844)



- 844 women at risk for breast cancer were followed prospectively for a median of 18 months.
- The median 25(OH)D concentration in this cohort was 50 ng/ml.
- Five of these women reported being diagnosed with breast cancer during the study period.
- Four of the five cases had 25(OH)D concentrations below 50 ng/ml.
- Those with concentrations ≥50 ng/ml had an 80% lower risk of breast cancer than those with concentrations <50 ng/ml, adjusting for age and BMI.

These findings suggest that 25(OH)D concentrations above 50 ng/ml may provide additional benefit in the prevention of breast cancer.

Chart Date: 4/17/14

 McDonnell SL et al., 25(OH)D serum levels ≥50 ng/ml may provide additional reduction in breast cancer risk. American Society of Nutrition Conference. April 2014.

Non-Skin Cancer Cases in the GrassrootsHealth and Lappe Cohorts (Women Ages 55+ Years)

GrassrootsHealth Cohort (N=1,135) and Lappe Cohort (N=1,169)

48 women in the Lappe cohort and 10 in the GrassrootsHealth cohort were diagnosed with cancer during the observation period.

The most common type of cancer was breast cancer.

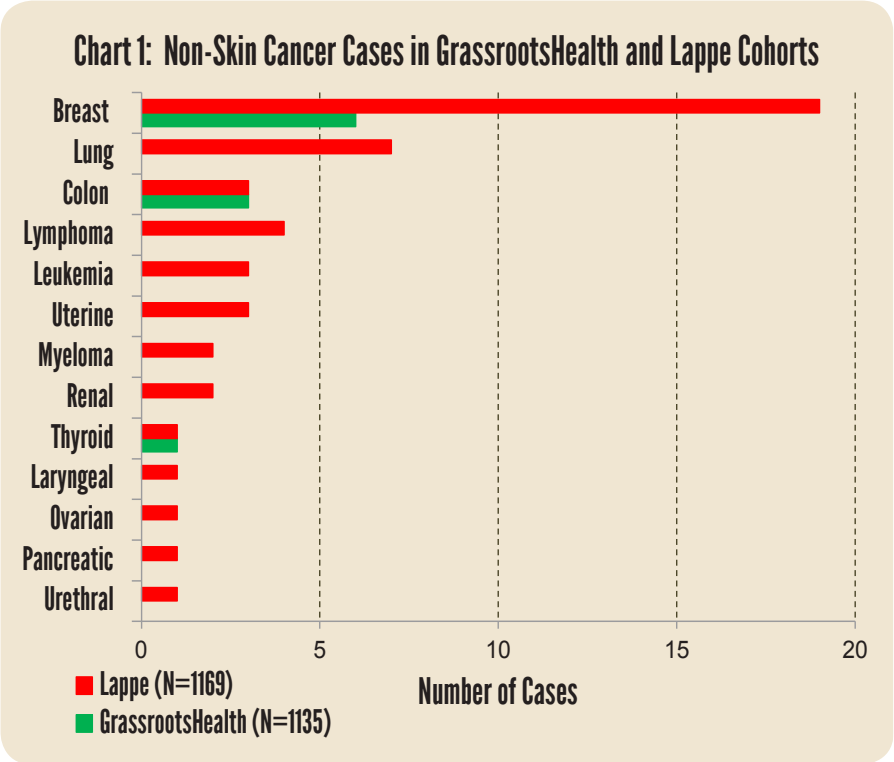


Chart Date: 10/8/15

 McDonnell SL, Baggerly C, French CB, Baggerly LL, Garland CF, Gorham ED, Lappe JM, Heaney RP. Serum 25-Hydroxyvitamin D Concentrations ≥40 ng/ml are Associated with >65% Lower Cancer Risk: Pooled Analysis of Randomized Trial and Prospective Cohort Study. PLoS One. 2016

Non-Skin Cancer Incidence Rates: GrassrootsHealth vs. Lappe Cohorts (Women Ages 55+ Years)

GrassrootsHealth Cohort (N=1,135) and Lappe Cohort (N=1,169)

Incidence rates of all non-skin cancers for the GrassrootsHealth cohort (median 25(OH)D = 48 ng/ml) and the Lappe cohort (median 25(OH)D = 30 ng/ml) were compared.

The incidence rate of cancer was 4.6 cases per 1,000 person-years in the GrassrootsHealth cohort and 11.3 cases per 1,000 person-years in the Lappe cohort (59% lower).

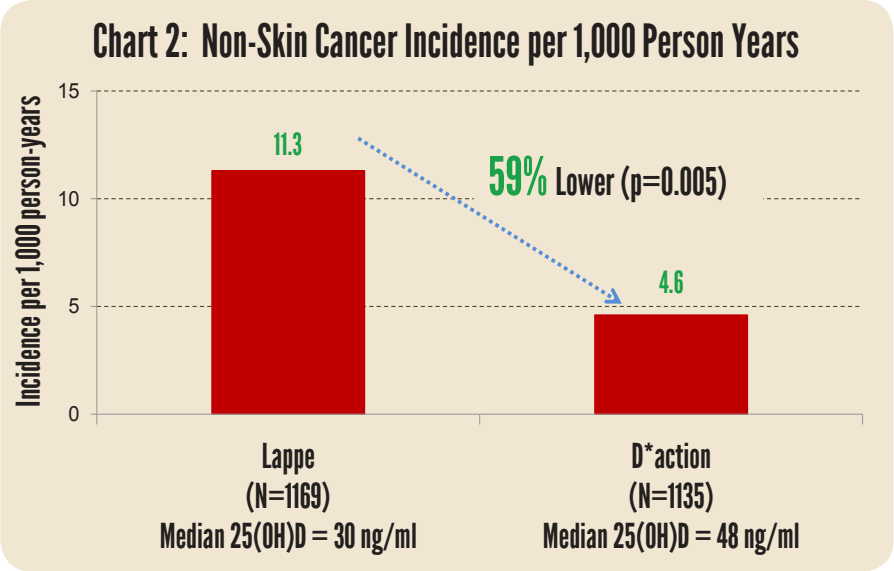


Chart Date: 10/1/15

 McDonnell SL, Baggerly C, French CB, Baggerly LL, Garland CF, Gorham ED, Lappe JM, Heaney RP. Serum 25-Hydroxyvitamin D Concentrations ≥40 ng/ml are Associated with >65% Lower Cancer Risk: Pooled Analysis of Randomized Trial and Prospective Cohort Study. PLoS One. 2016

Kidney Stones and Diabetes

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

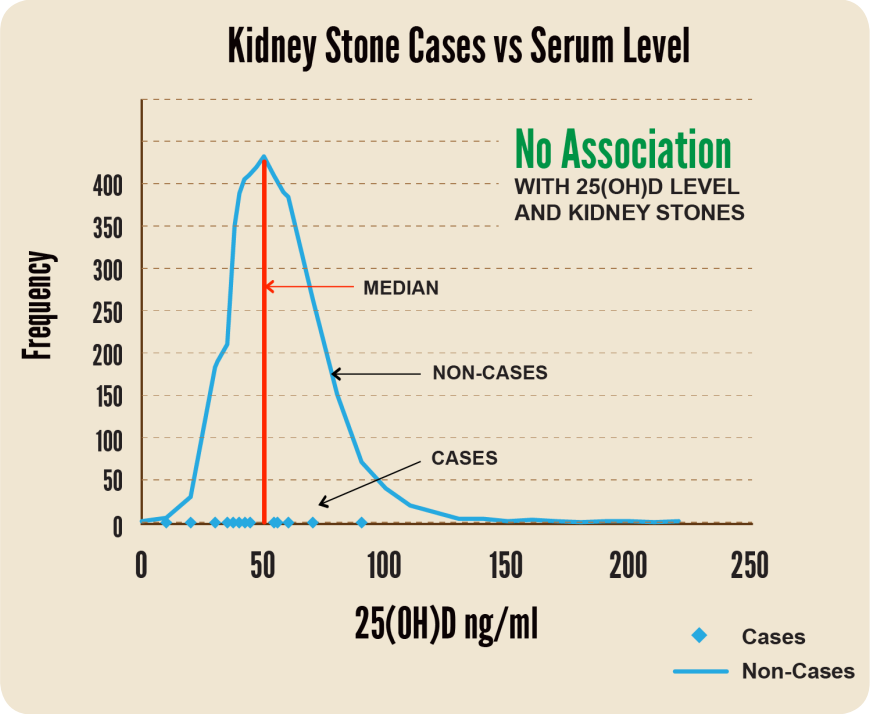
Frequency Distribution of 25(OH)D among Cases and Non-Cases of Kidney Stones

GrassrootsHealth D*action Cohort (N=2,012)

Of 2,012 D*action participants who had submitted at least two health questionnaires and vitamin D blood tests, 13 indicated an occurence of kidney stones after their first test.

Of the 13 cases, eight were below the median serum level of 50 ng/ml and five were above.

No association was found between serum 25(OH)D in the range of 20-100 ng/ml and incidence of kidney stones.



Individuals with a body mass index (BMI) of ≥ 30 had a 3-fold higher risk of developing kidney stones.

Chart Date: 10/1/13

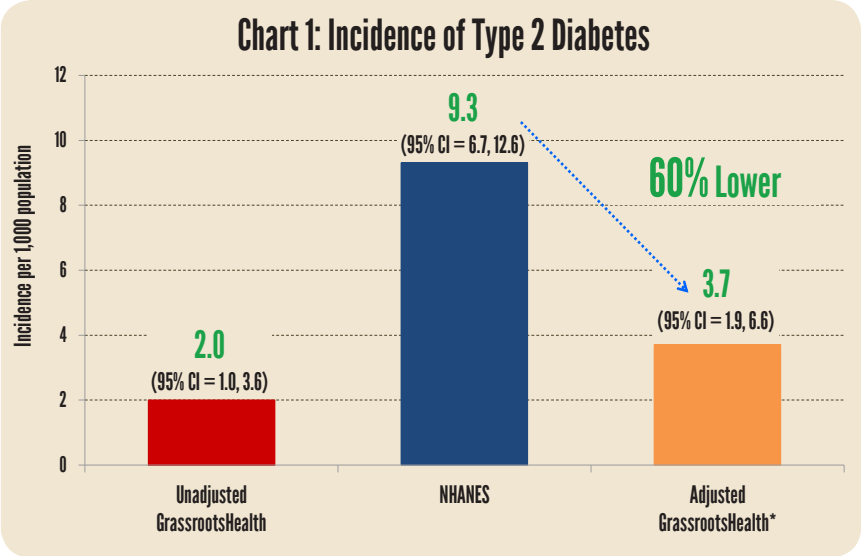
 Nguyen, S., Baggerly, L.L., French, C., Heaney, R.P., Gorham, E.D., Garland, C.F. (2013) 25-Hydroxyvitamin D in the Range of 20 to 100 ng/mL and Incidence of Kidney Stones. *American Journal of Public Health*, online ahead of print, 10/17/2013.

Incidence Rate of Type 2 Diabetes is >50% Lower in GrassrootsHealth vs. NHANES (Participants Ages 20+ Years)

GrassrootsHealth (N=4,933) and NHANES (N=4,078)

This study compared incidence rates of type 2 diabetes among participants aged ≥20 years in two U.S. cohorts with markedly different median 25(OH)D concentrations.

The median 25(OH)D concentration in the GrassrootsHealth cohort was 41 ng/ml while in the 2005-6 NHANES it was 22 ng/ml.



The adjusted annual incidence rate of type 2 diabetes was 3.7 per 1,000 population in the GrassrootsHealth cohort, compared to 9.3 per 1,000 population in NHANES (60% lower).

Chart Date: 8/13/14

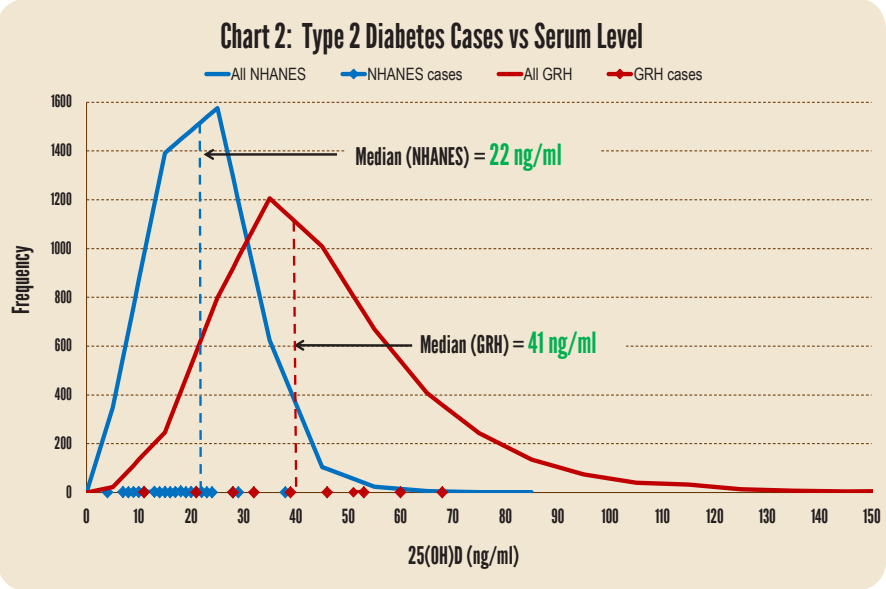
 McDonnell SL et al., Incidence rate of type 2 diabetes is >50% lower in GrassrootsHealth cohort with median serum 25-hydroxyvitamin D of 41ng/ml than in NHANES cohort with median of 22ng/ml. J Steroid Biochem Mol Biol. 2016 Jan;155(Pt B):239-44.

Incidence Rate of Type 2 Diabetes is >50% Lower in GrassrootsHealth vs. NHANES (Participants Ages 20+ Years)

GrassrootsHealth D*action Cohort (N=4,933) and NHANES (N=4,078)

Among the 10 individuals who developed diabetes in the GrassrootsHealth cohort, 5 were below the median cohort serum level of 41 ng/ml and 5 were equal to or above it.

Among the 38 individuals who developed diabetes in the NHANES cohort, 31 were below the median cohort serum level of 22 ng/ml and 7 were equal to or above it.



These findings support the previously found association between higher serum 25(OH)D levels and a reduced risk of type 2 diabetes.

Chart Date: 8/13/14

Symptoms

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Pain Rating vs Serum Level

GrassrootsHealth D*action Cohort (N=5,823)

Just over 60%* of all D*action participants report pain of some type.

The average pain rating for participants with a serum level below 20 ng/ml was 5.2.

Participants with a serum level greater than 80 ng/ml reported pain levels at an average of 4.6, a 12% decrease.

In addition to overall pain rating, there was also a specific 20% reduction in back pain.

*5823 Total
3588 With Pain

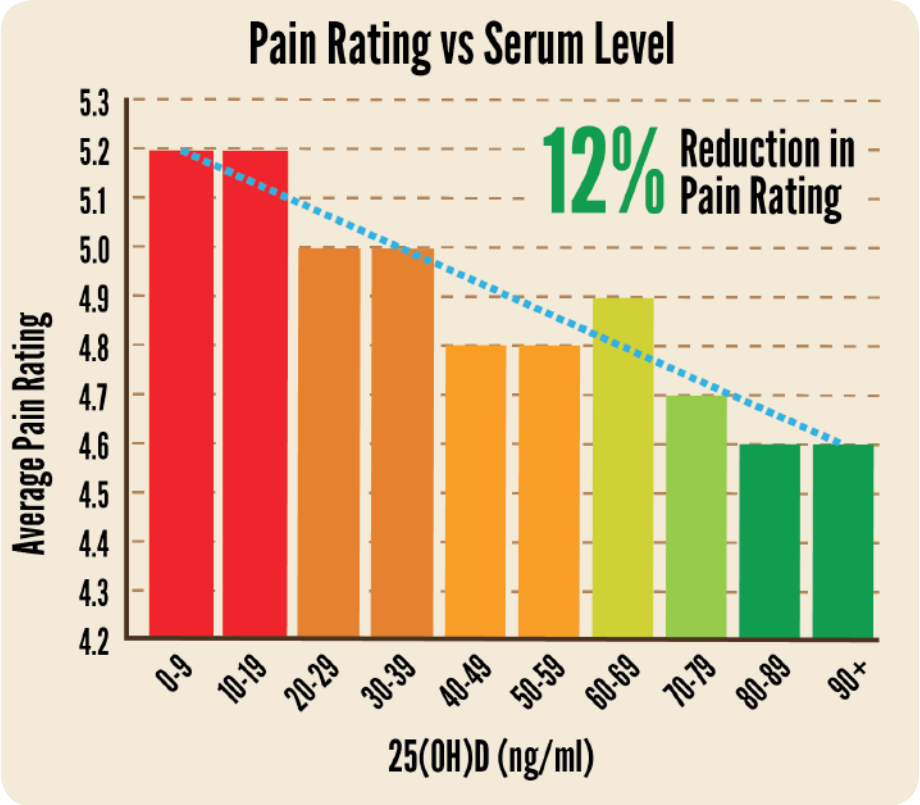


Chart Date: 2/1/2013

Experienced a Cold or Flu in Prior 6 Months by Vitamin D Status

GrassrootsHealth D*action Cohort (N= 8,695)

33% of participants experienced a cold and 10% experienced a flu during the 6 months before their most recent test.

Participants with vitamin D levels ≥40 ng/ml reported 41% fewer cases of the flu and 15% fewer colds compared to participants with levels <20 ng/ml.

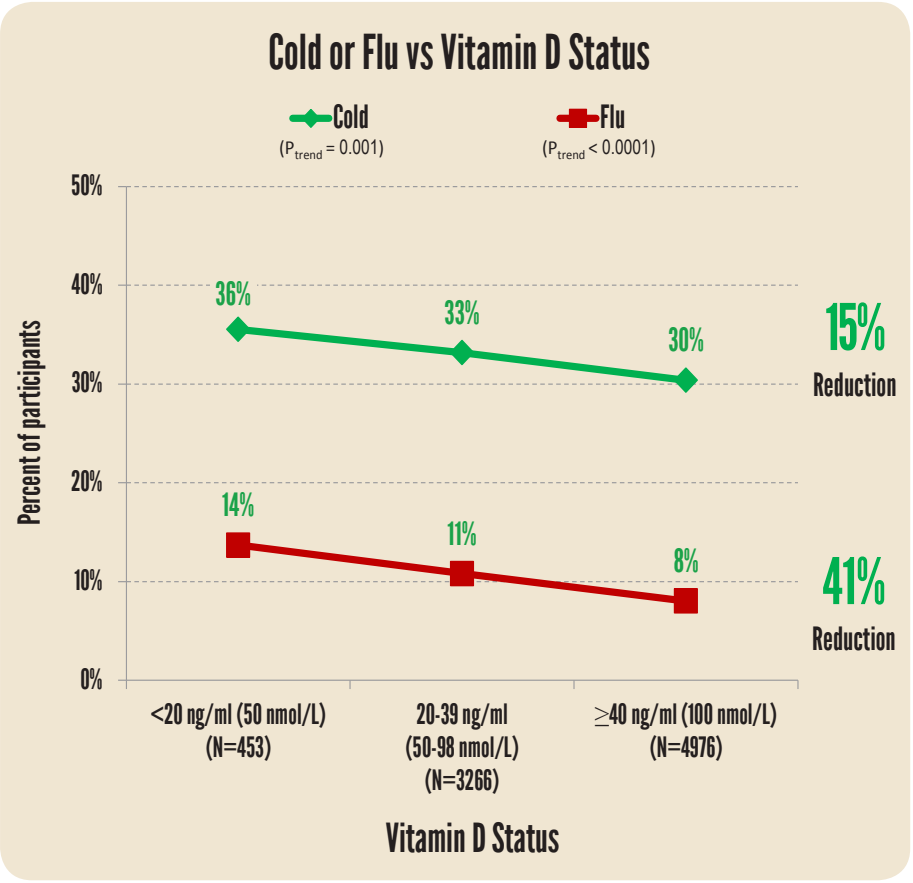


Chart Date: 8/31/15

Experienced a Broken Bone in Prior 6 Months by Vitamin D Status (Ages 65+ years)

GrassrootsHealth D*action Cohort (N=1,659)

Those who broke a bone were more likely to have a serum level <40 ng/ml than ≥40 ng/ml.

Those with serum levels <20 ng/ml had 3 times the risk of breaking a bone compared to those ≥40 ng/ml.

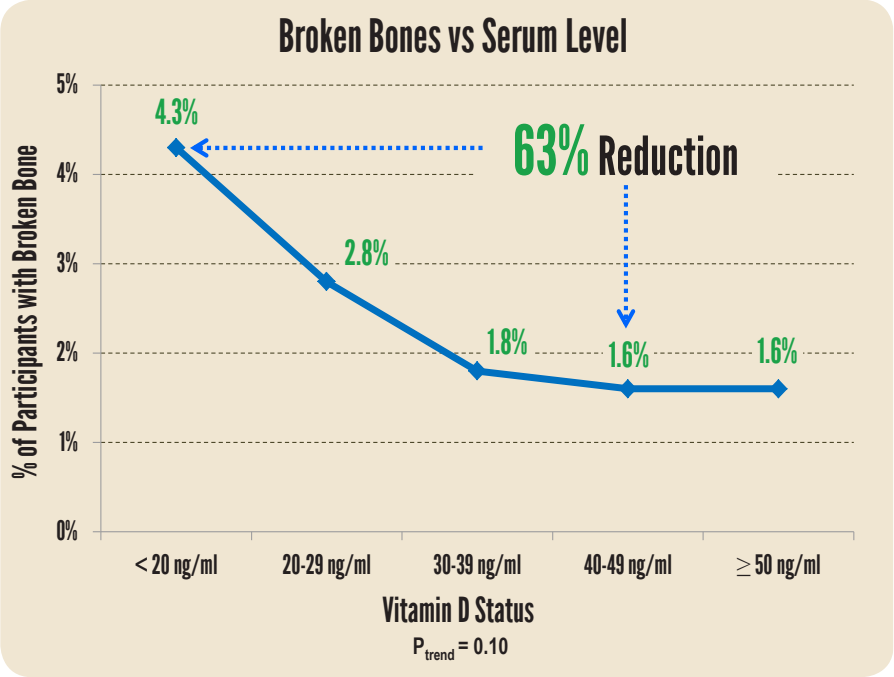


Chart Date: 4/24/15

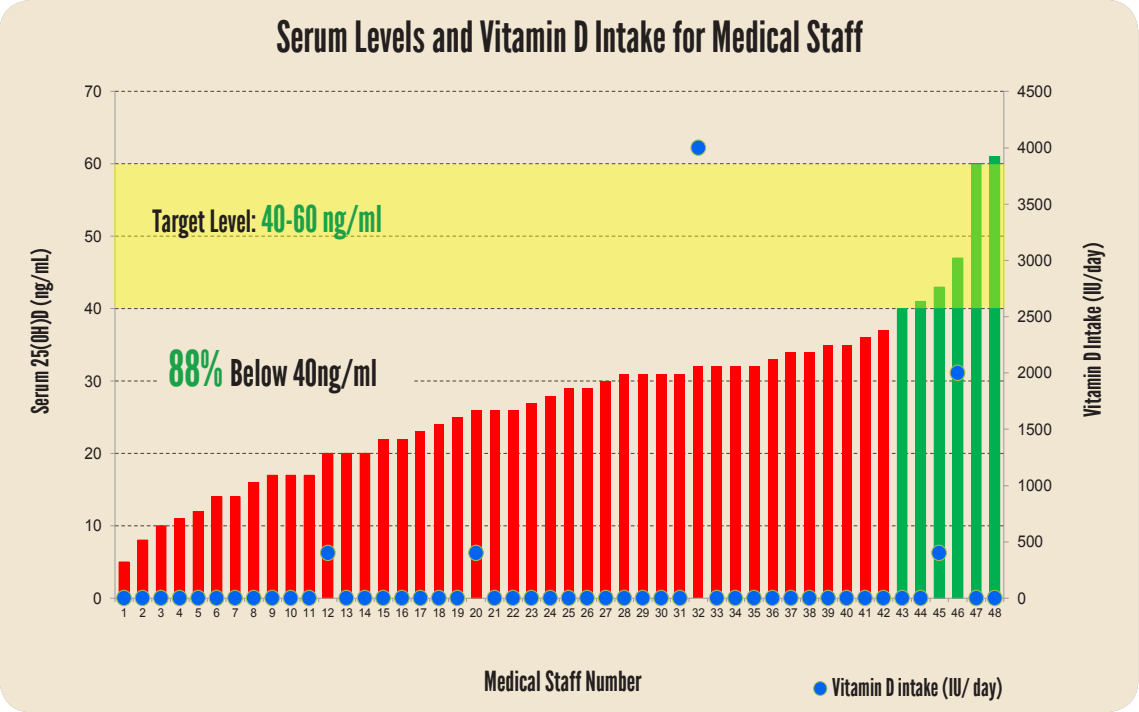
Population Groups

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Initial 25(OH)D Measurements and Vitamin D Intake for Medical Staff Members

Medical Staff (N=48)



A majority (88%) of the medical staff had 25(OH)D concentrations <40 ng/ml on their initial test.

Also, a majority (90%) of the medical staff reported not taking vitamin D supplements.

Chart Date: 10/12/15

Initial 25(OH)D Concentrations and Vitamin D Intake Amounts for "Vitamin D for Public Health" Seminar Participants

GrassrootsHealth December 2014 Seminar Participants (N=24)

Less than half of the seminar participants (42%) had 25(OH)D concentrations ≥40 ng/ml on their initial test.

The median vitamin D supplement intake amount was 1500 IU/day.

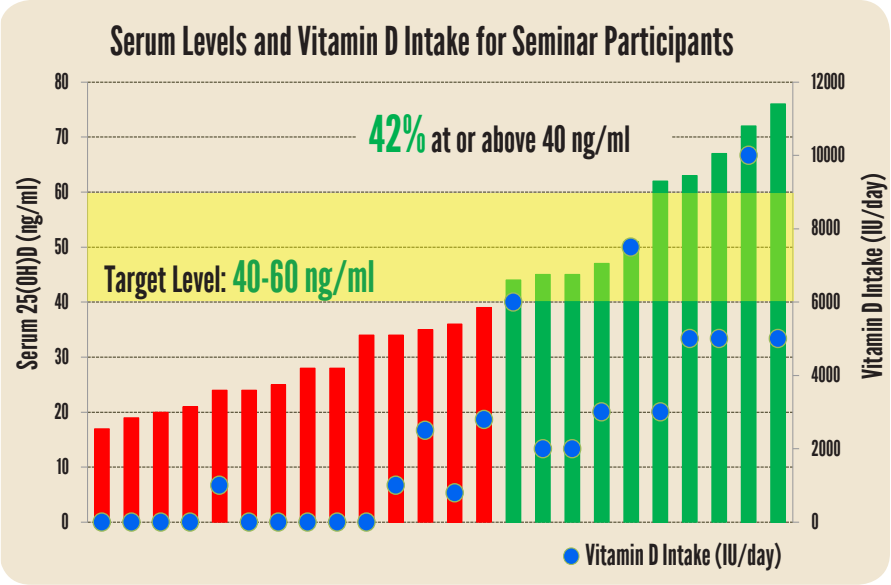


Chart Date: 9/22/15

End of Summer 25(OH)D Measurements for Southern California Lifeguards

Southern California Lifeguards (N=13)

A majority of the lifeguards (62%) had 25(OH)D concentrations ≥40 ng/ml.

All of the lifeguards reported not taking any vitamin D supplements.

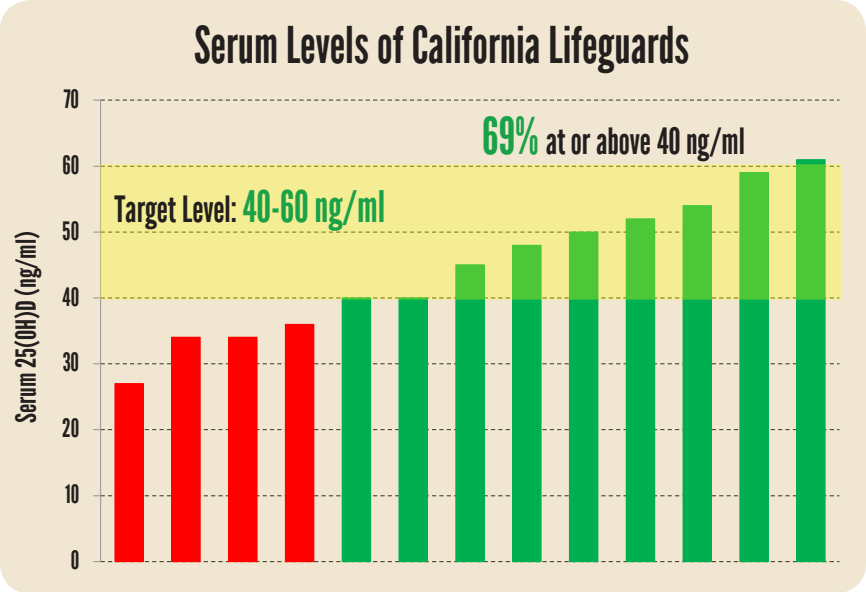


Chart Date: 10/28/15

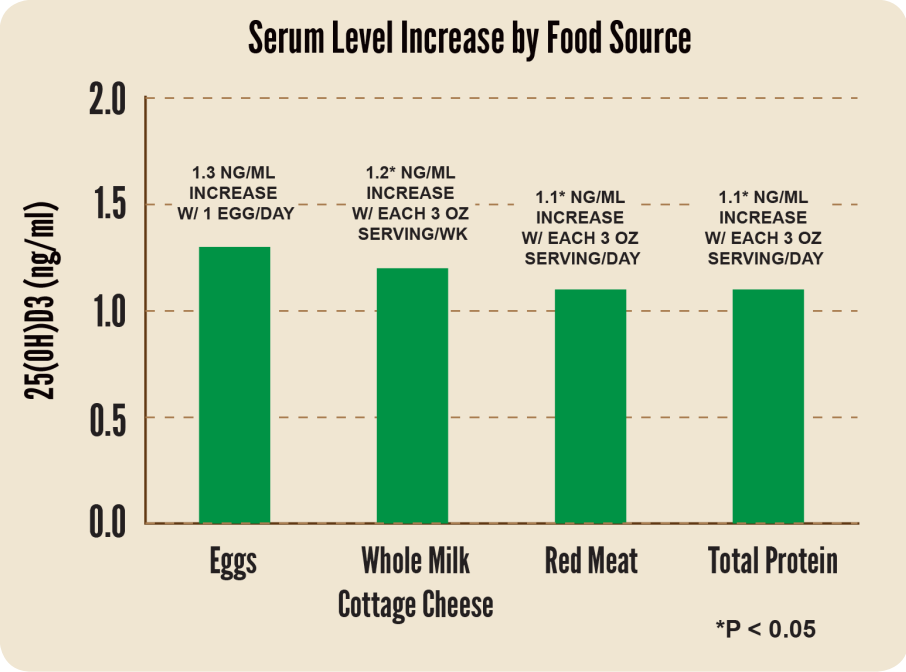
Extended Characteristics

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Serum 25(OH)D3 Increase for Each Food Source

GrassrootsHealth D*action Cohort (N=640)



From 780 non-supplement taking, adult, D*action participants who completed a limited questionnaire on dietary intake along with a lifestyle questionnaire, some food sources were found to be associated with vitamin D serum levels: eggs, whole milk cottage cheese, red meat and total protein. 25(OH) D3 rose by about 1 ng/ml for each weekly serving of whole milk cottage cheese (3 oz) and each daily serving of one of the following: eggs (1 egg), red meat (3 oz) and total protein (3 oz).

Non-food factors associated with vitamin D serum levels (not shown in the chart) were indoor tanning use, sun exposure, body mass index (BMI), and percent of work performed outdoors. The ability of non-food and food sources to explain inter-individual variability was limited, therefore supplementation will likely be key to improving vitamin D status on a population level.

Chart Date: 12/1/13

 McDonnell, S.L., French, C.B., Heaney, R.P. (2013) "Quantifying the non-food sources of basal vitamin d input" and "Quantifying the food sources of basal vitamin d input" *J Steroid Biochem Mol Biol.*, online ahead of print 10/28/13 and 11/1/13, respectively.

Serum Level by Sun Exposure Amount for Non-Supplement Takers

GrassrootsHealth D*action Cohort (N=1,543)

Average daily amount of time spent outdoors with sun-exposed skin between 10am-2pm during the prior 6 months.

In D*action participants who reported taking no vitamin D supplements, vitamin D serum levels rose by about 1.2 ng/ml for each additional 15 minutes per day spent outdoors in the sun with exposed skin.

Of special note is that the 2-4 hour group (outdoor worker type) achieved the recommended 40 ng/ml (100 nmol/L) observed in outdoor worker populations.

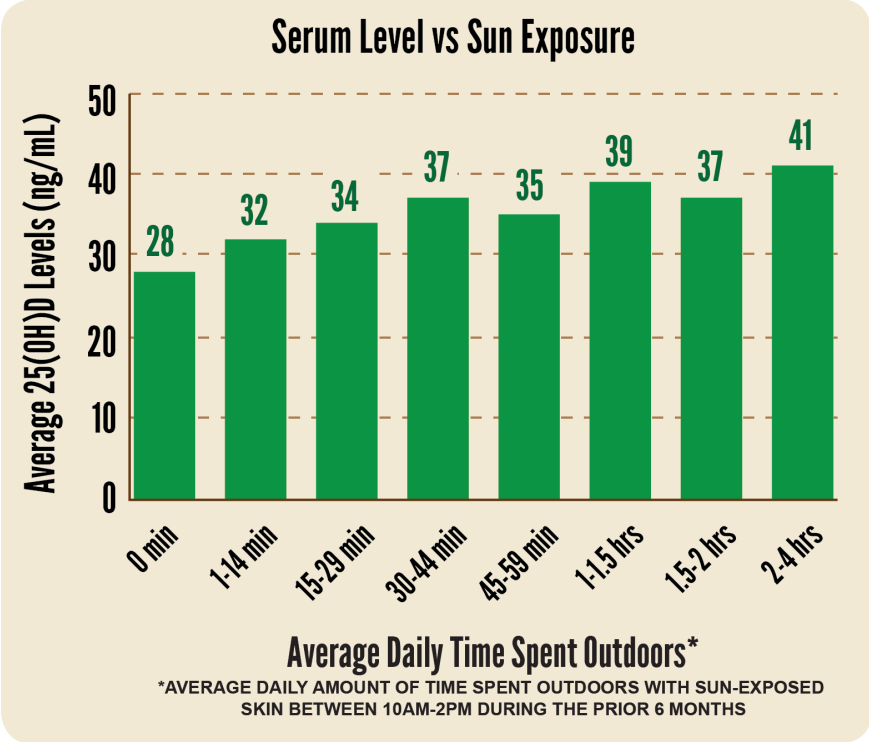


Chart Date: 7/1/13

Percent of Participants per Reported Vitamin D Supplement Type

GrassrootsHealth D*action Cohort (N=2,250)

Gel-caps are the most popular form of vitamin D supplements among D*action participants, while powder is the least popular.

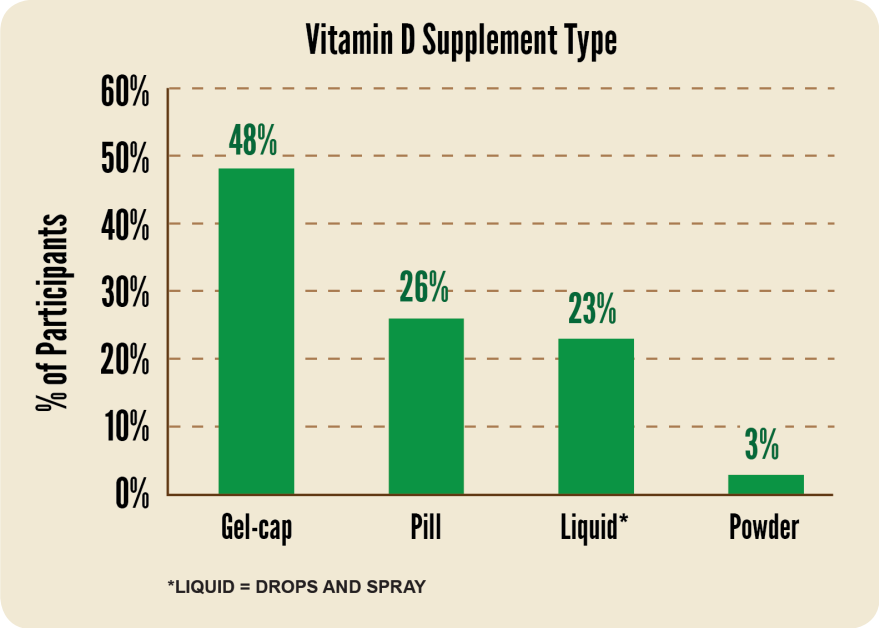


Chart Date: 7/11/13

Average Vitamin D Serum Level by Reported Supplement Type and Intake Amount

GrassrootsHealth D*action Cohort (N=1,161)

While there may be differences for a given individual, there does not appear to be an overall difference in the average serum level between supplement types.

*Powder had too few participants for 2000, 4000, and 10,000 IU to produce a reliable estimate.

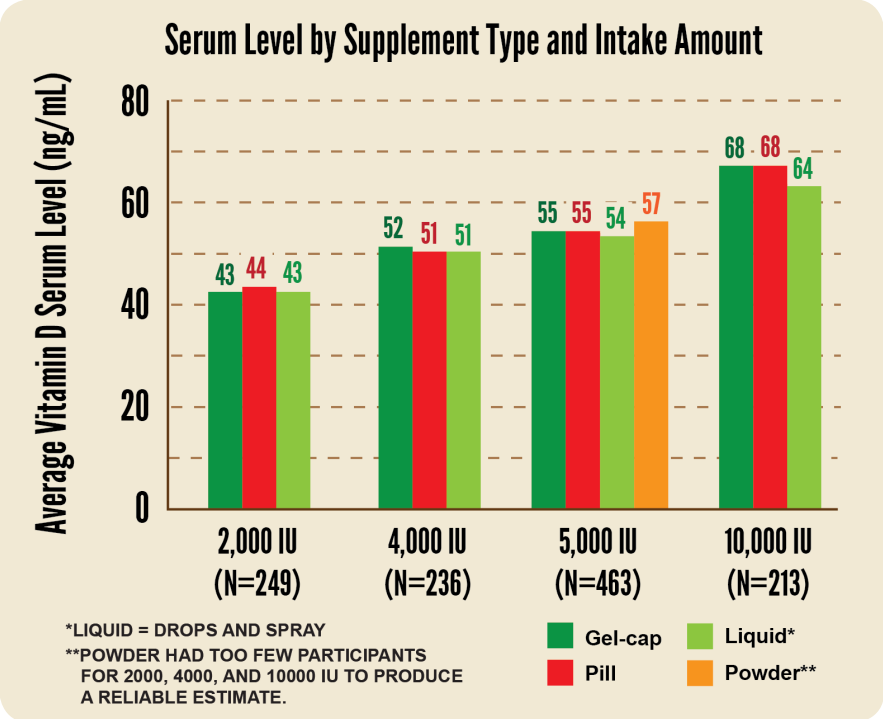


Chart Date: 7/11/13

Average Serum Level by Vitamin D Supplement Amount (Ages 18+ Years)

GrassrootsHealth D*action Cohort (N=9,014)

As supplement intake amounts increased, average 25(OH)D concentrations increased (from 28 ng/ml for those taking no supplements to 70 ng/ml for those taking 10,000 IU/day or more).

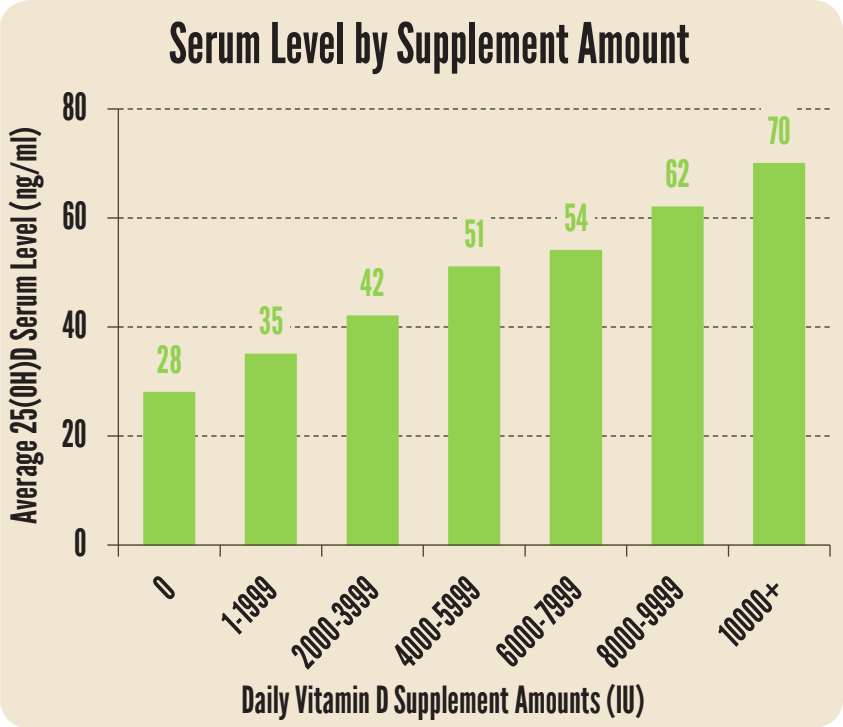


Chart Date: 1/18/16

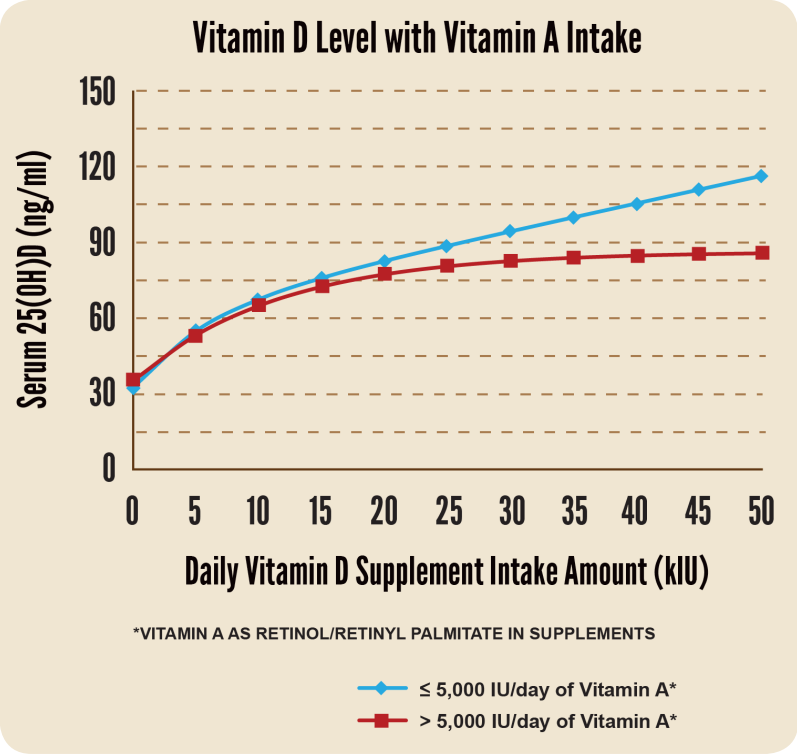
Vitamin D Dose Response Curves for Vitamin A Intake Amounts

GrassrootsHealth D*action Cohort (N=3,355)

Evidence suggests that excess vitamin A (as retinol or retinyl palmitate) can bind to the vitamin D receptor and partially block vitamin D action. This is of particular interest as high intakes of vitamin A may actually limit the increase of vitamin D serum levels.

In a preliminary analysis of the D*action data, we found 34% of participants report taking vitamin A as retinol or retinyl palmitate in supplements.

Of those who take vitamin A, the average amount is 5,400 IU per day.



Participants who take more than 5,000 IU of vitamin A per day have a lower vitamin D dose response than those who take 5,000 IU or less.

Chart Date: 7/26/13

Physical Activity Among D*action Participants

GrassrootsHealth D*action Cohort (N=7,566)

More than 90% of GrassrootsHealth participants report some level of regular exercise.

About half engage in mild or moderate activity and one third engage in strenuous activity.

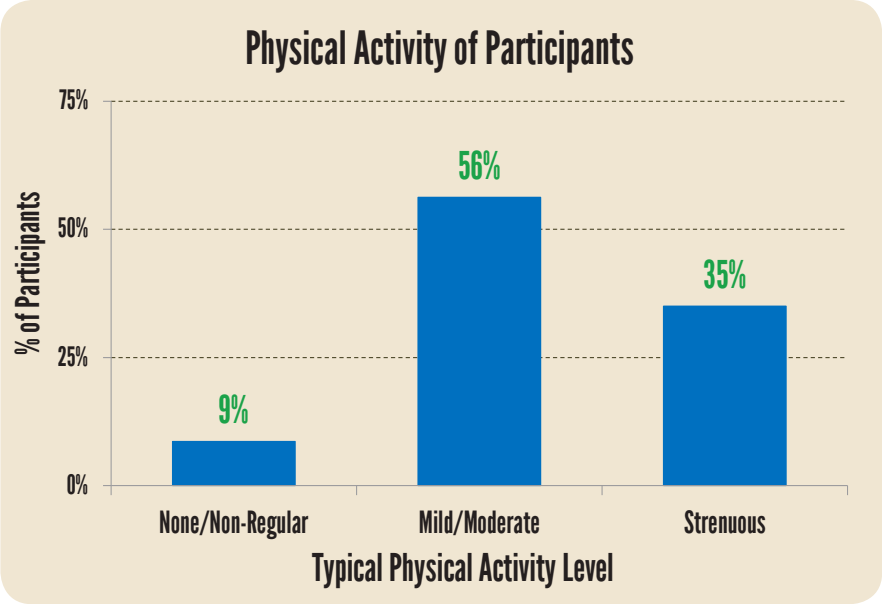


Chart Date: 4/28/15

Dose Response by Physical Activity Level

GrassrootsHealth D*action Cohort (N=7,566)

We charted dose response curves (intake vs. serum level) by level of physical activity.

Regular exercisers have a slightly higher vitamin D dose response than non-regular exercisers, especially in the lower dose range.

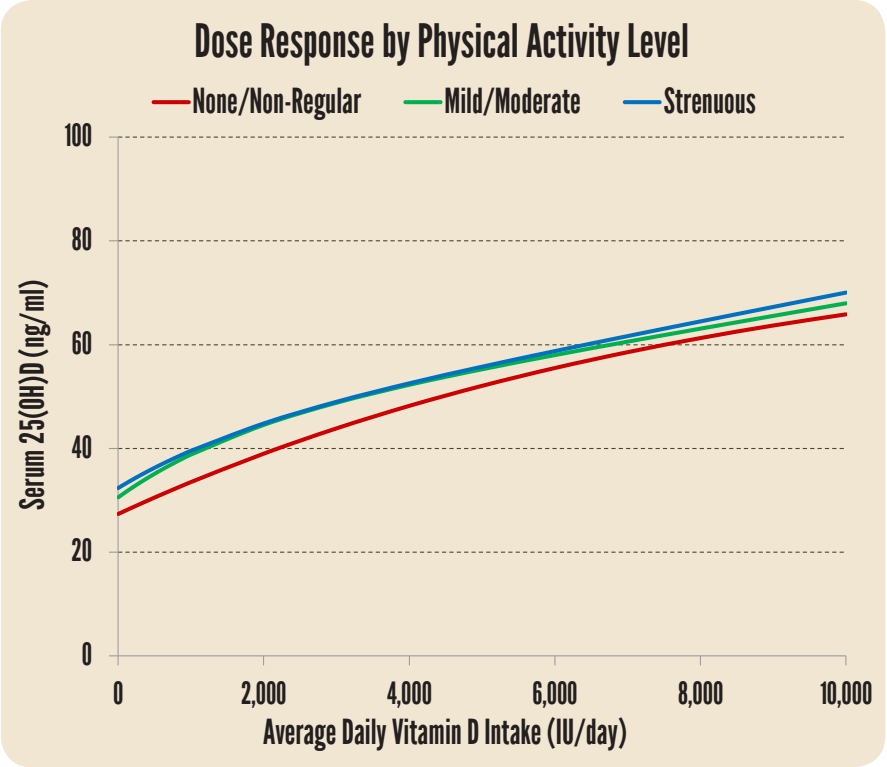


Chart Date: 4/28/15

Vitamin D Supplement Intake by Age

GrassrootsHealth D*action Cohort (N=6,967)

The percent of participants taking vitamin D supplements increased as age increased (from 69% for those 15-34 years to 91% for those 65 years and older).

The median vitamin D intake amount increased as age increased (from 3500 IU/day for those 15-34 years to 4300 IU/day for those 65 years and older).

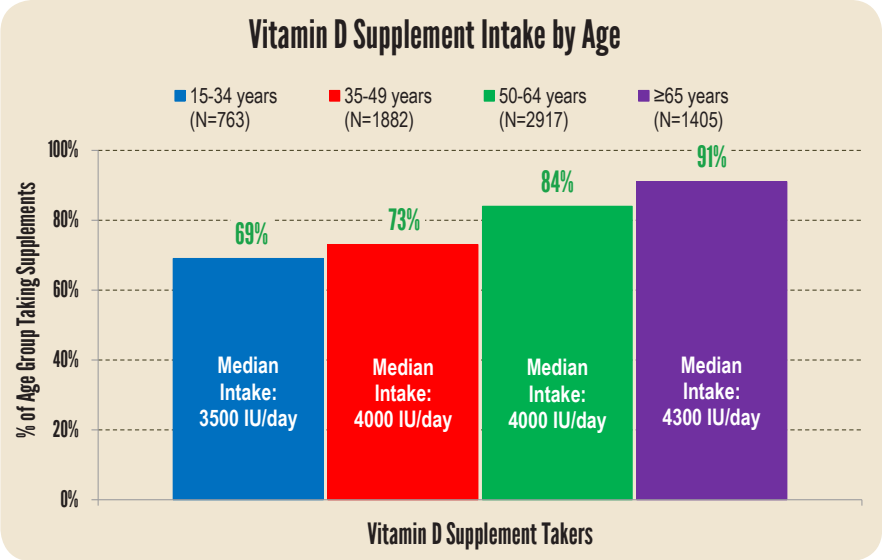
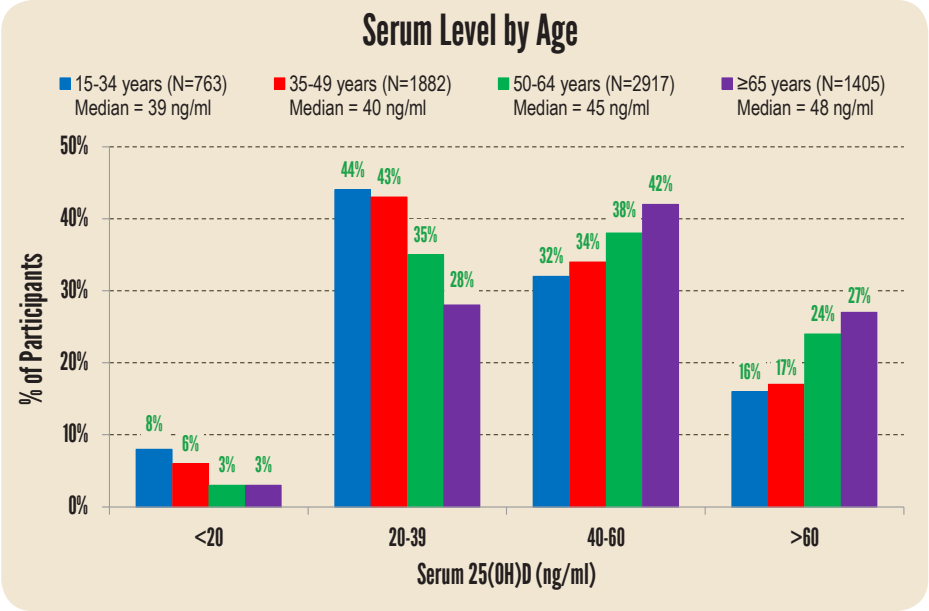


Chart Date: 10/22/14

Vitamin D Serum Level by Age

GrassrootsHealth D*action Cohort (N=6,967)

Median serum concentration increased by age, from 39 ng/ml for those 15-34 years old to 48 ng/ml for those 65 years and older.



The proportion of those with serum concentrations ≥40 ng/ml increased as age increased (48% for those 15-34 years, 51% for those 35-49 years, 62% for those 50-64 years, and 69% for those 65 years and older).

There was no difference in dose response by age.

Chart Date: 10/23/14

Vitamin D Serum Level by Gender

GrassrootsHealth D*action Cohort (N=7,123)

Two-thirds of D*action participants are female (64%) and one-third are male (36%).

The percent of participants taking vitamin D supplements is the same for both genders (80%). Also, the median intake is the same for both genders (4000 IU/day).

The median serum level is similar between males (45 ng/ml) and females (43 ng/ml).

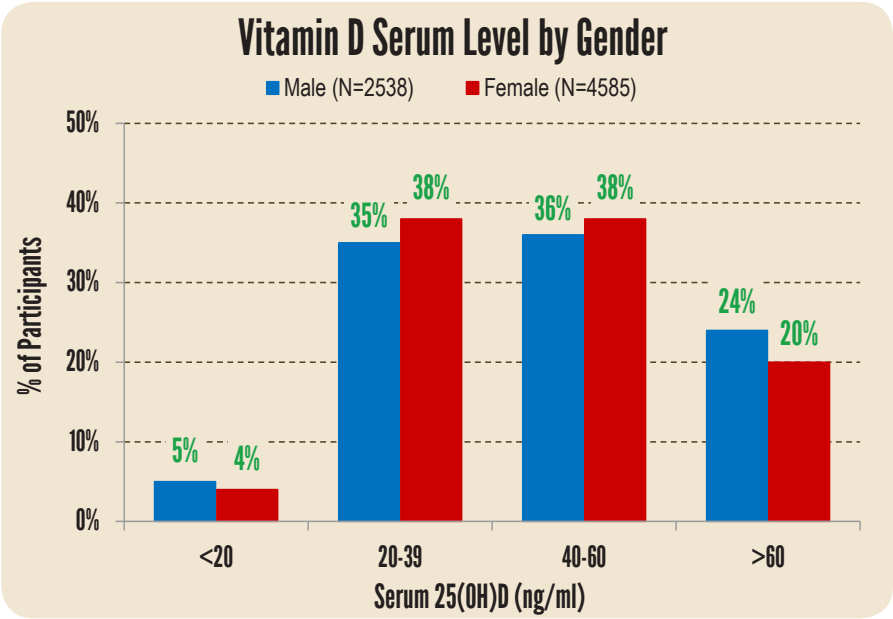


Chart Date: 10/10/14

Vitamin D Supplement Intake by Latitude

GrassrootsHealth D*action Cohort (N=7,123)

The median latitude for the GrassrootsHealth cohort is +/- 40 degrees.

Supplement intake is consistent across latitude with approximately 80% of participants taking vitamin D supplements.

The median intake is the same across latitude (4000 IU/day).

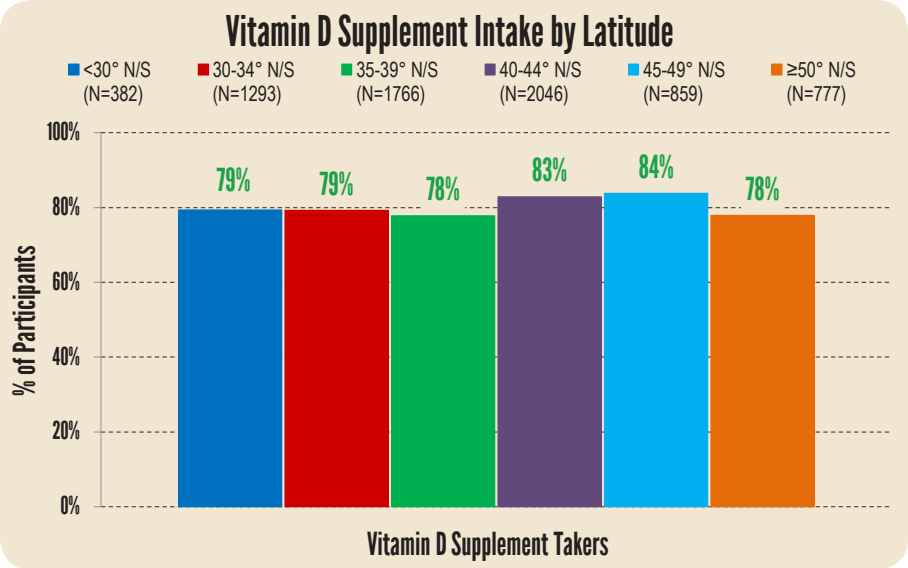


Chart Date: 10/23/14

GrassrootsHealth
Moving Research into Practice

www.grassrootshealth.net

Vitamin D Serum Level by Latitude

GrassrootsHealth D*action Cohort (N=7,123)

Median serum concentration was similar across latitude for all participants (~43 ng/ml) and among non-supplement takers (~30 ng/ml).

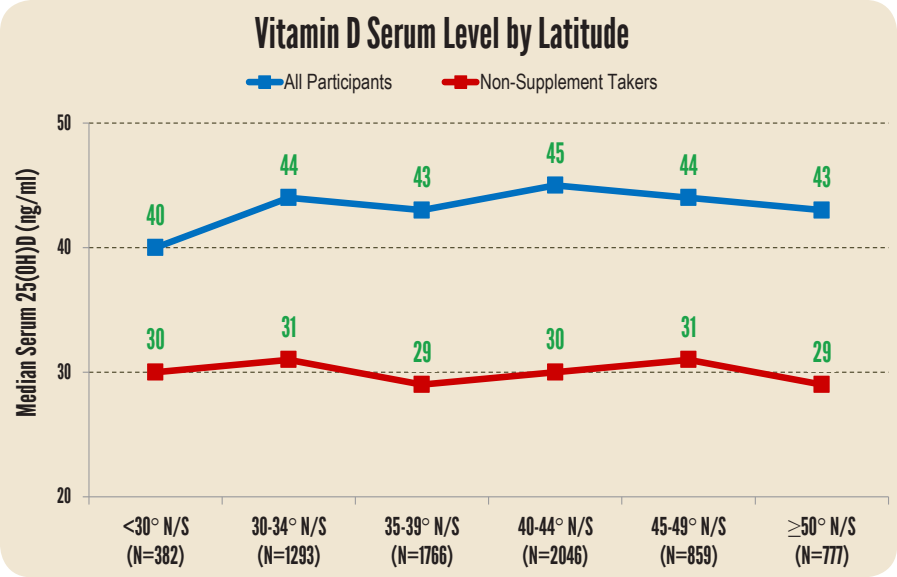


Chart Date: 10/23/14

Vitamin D Supplement Intake by Percent Outdoor Occupation

GrassrootsHealth D*action Cohort (N=6,808)

As the percentage of work performed outdoors increased, the percentage of participants taking supplements decreased (from 82% for those who perform none of their occupation outdoors to 71% for those who perform >50% of their occupation outdoors).

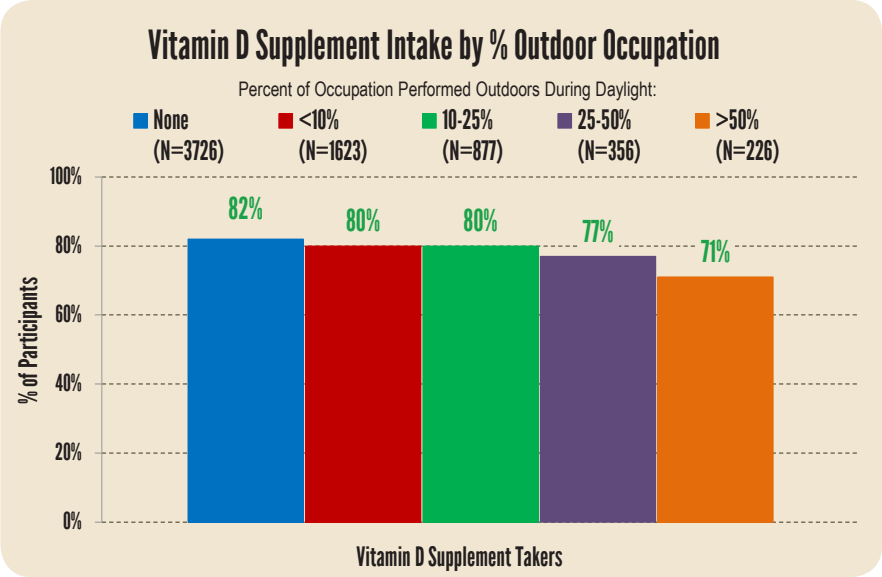


Chart Date: 10/23/14

Percent of Occupation Performed Outdoors During Daylight

GrassrootsHealth D*action Cohort (N=6,808)

A majority (79%) of D*action participants perform <10% of their occupation outdoors.

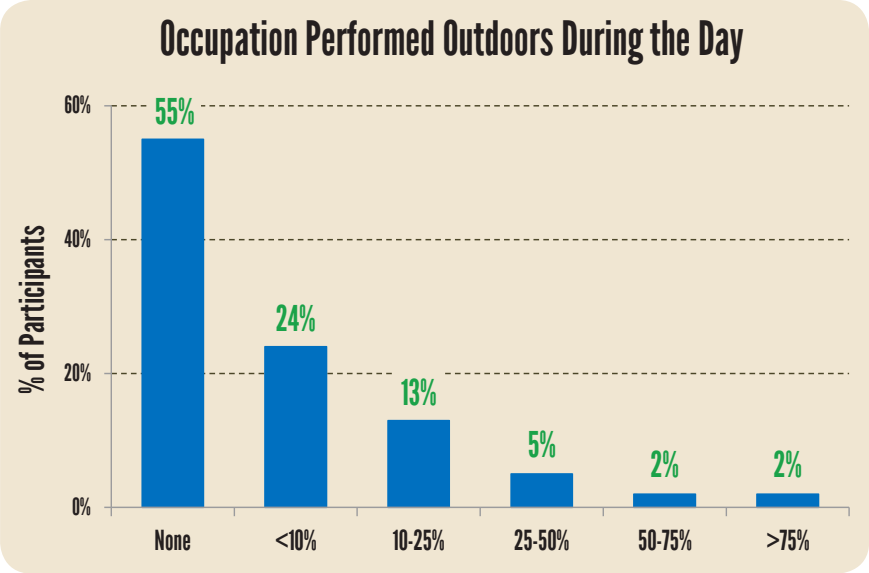


Chart Date: 10/23/14

Median Vitamin D Intake by Month of Year*

GrassrootsHealth D*action Cohort (N=6,814)

For participants' first test, the annual average vitamin D intake amount was 1600 IU/day and the average serum level was 40 ng/ml.

For those who tested at least twice, the annual average intake amount for the second test was 4000 IU/day and the average serum level was 47 ng/ml.

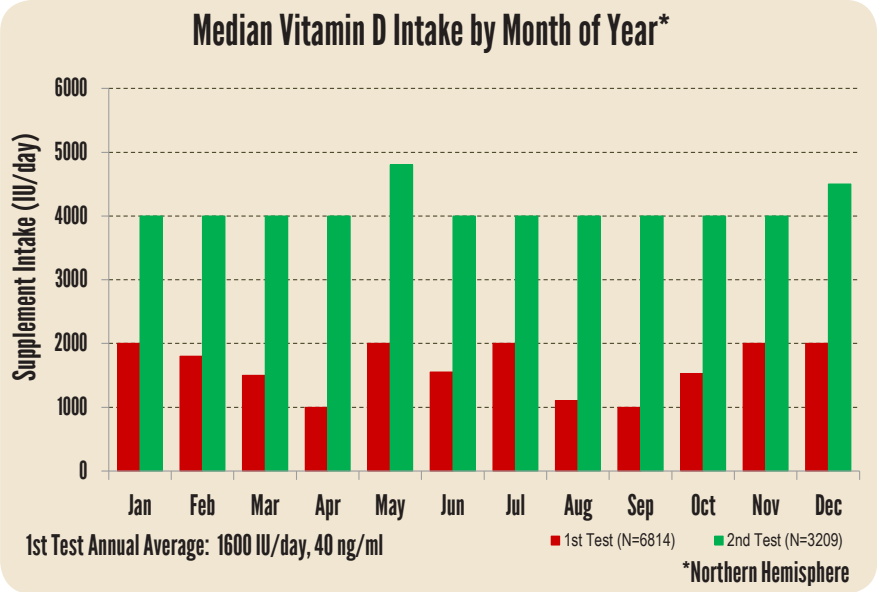
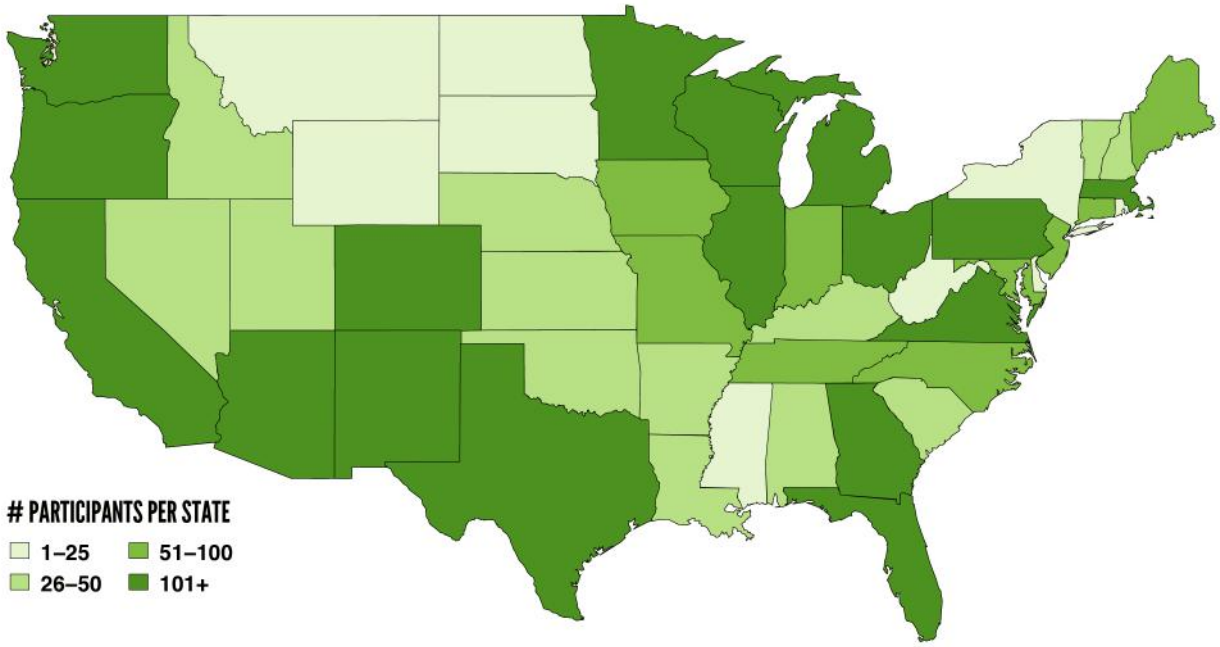


Chart Date: 4/2/14

D*action Participant Counts in the United States

GrassrootsHealth D*action Cohort (N=4,888)



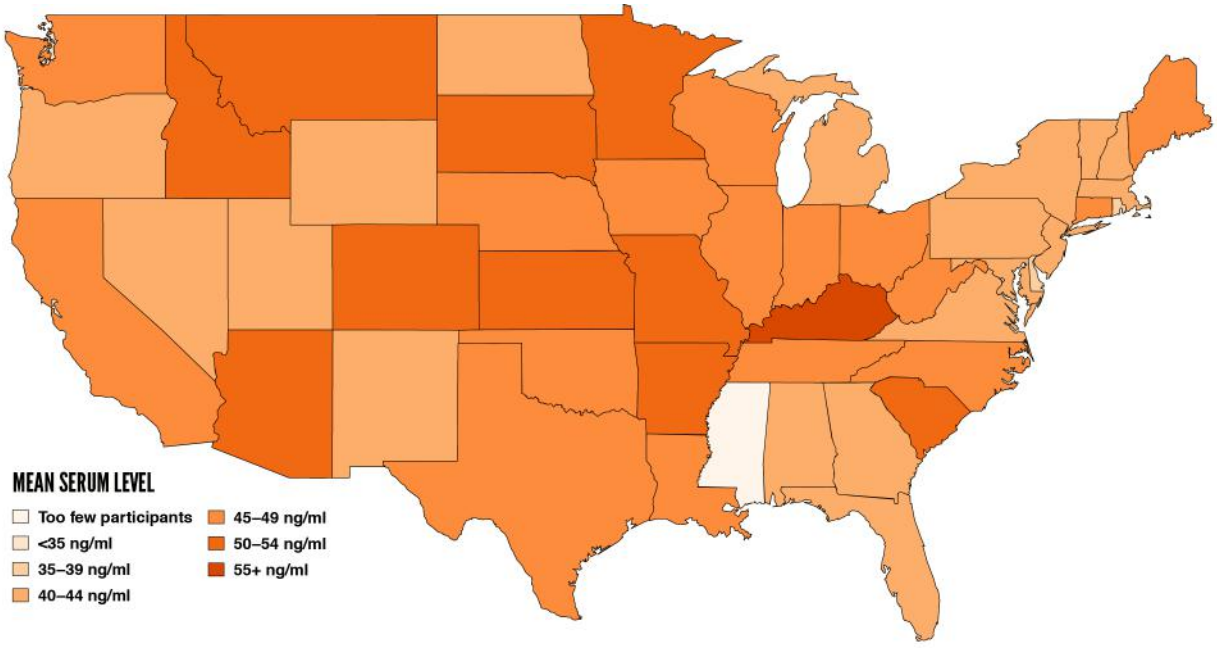
Not pictured: Alaska:39; Hawaii:18; Washington DC:6

80% of the D*action participants live in the U.S. with 26 states having more than 50 participants and 17 states having more than 100 participants.

Chart Date: 7/5/13

D*action Vitamin D Serum Levels in the United States

GrassrootsHealth D*action Cohort (N=4,888)



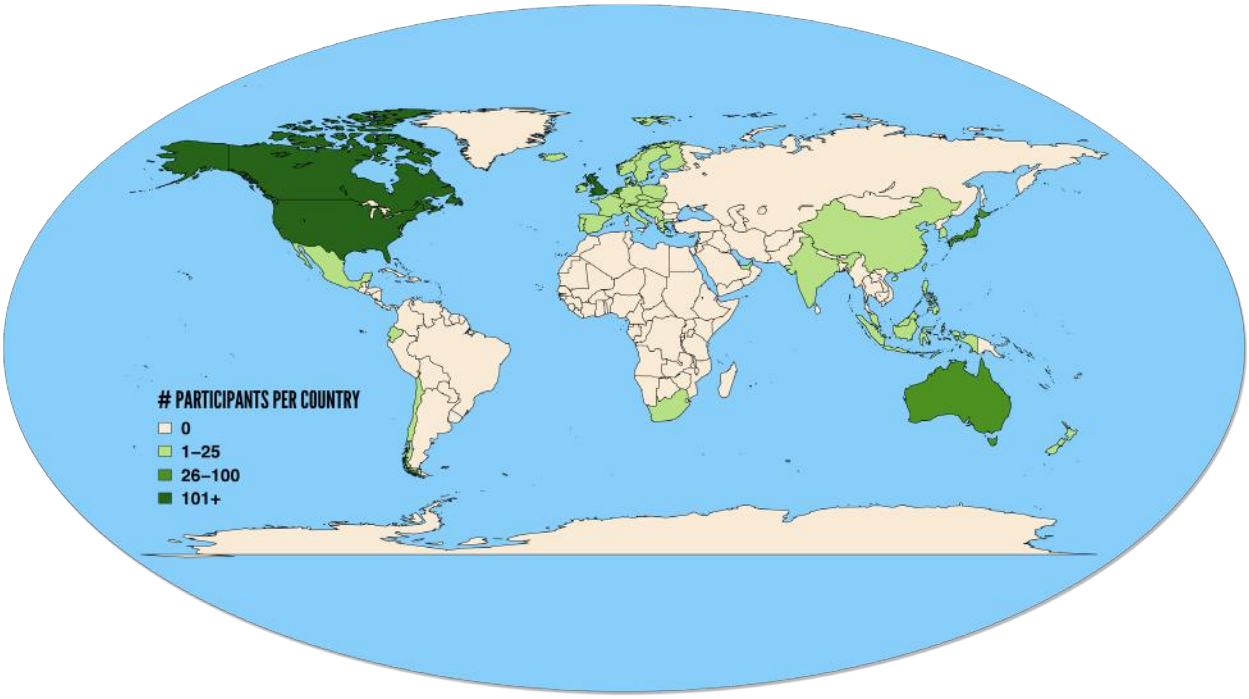
Alaska: 52.03 ng/ml; Hawaii: 42.17 ng/ml.

Across the U.S., the average vitamin D serum level by state ranged from 35 ng/mL (Delaware) to 55 ng/mL (Kentucky) with an overall average serum level of 46 ng/mL. (Vitamin D serum levels are from participants' first samples provided.)

Chart Date: 7/5/13

D*action Around the World

GrassrootsHealth D*action Cohort (N=6,125)



D*action has participants in 45 countries on every inhabited continent.
Of the non-US residing participants, 46% live in Canada, 30% live in Great Britain, 4% live in Australia, 4% live in Japan, 2% live in the Netherlands, and 14% live in other countries.

Chart Date: 7/5/13