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Vitamin D Supplementation and Screening for the Prevention of Rickets and Osteomalacia in Alaska

Recommendations from the Alaska Vitamin D Workgroup

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Executive Summary

Prompted by Alaska's elevated rate of rickets and unique risk factors for vitamin D deficiency, in November 2017, the Alaska Division of Public Health assembled a team of health care providers and vitamin D subject matter experts to form the Alaska Vitamin D Workgroup. The goals of the Workgroup are to a) review and evaluate the scientific evidence regarding the roles of vitamin D in human health, b) review Alaska's unique risk factors for vitamin D deficiency and rickets, and c) determine if Alaska-specific supplementation screening vitamin D or recommendations are warranted to prevent rickets and other conditions demonstrated to be caused by vitamin D deficiency, such as osteomalacia.

The Workgroup reviewed medical literature on vitamin D and analyzed studies specific to Alaska and other Arctic countries during two in-person meetings that were held in December 2017 and February 2018. Proposed Alaska-specific vitamin D recommendations were subsequently presented at pediatric and internal medicine grand rounds in Anchorage for professional comment. Upon review, the Workgroup concluded that increased vitamin D supplementation for infants and pregnant women, beyond current national guidelines, should be considered to prevent rickets in Alaska children.

The Workgroup's recommendations regarding vitamin D supplementation for the prevention of rickets are as follows:

- Clinicians should consider supplementing exclusively or partially breastfed infants with 800 IU/day of vitamin D.
- Clinicians should continue supplementing all infants who are exclusively formula-fed with 400 IU/day of vitamin D *in addition to* the 400 IU/liter of vitamin D contained in their formula.
- Clinicians should consider supplementing pregnant women in Alaska with 1,000 IU/day of vitamin D *in addition to* the 400 IU/day of vitamin D contained in their daily prenatal vitamins.

At this time, there is insufficient cost-effectiveness evidence to recommend screening healthy infants and pregnant women for vitamin D deficiency to prevent rickets; therefore, the Alaska Vitamin D Workgroup does not recommend universal screening of infants or pregnant women for vitamin D deficiency for the prevention of rickets.

At this time, there is insufficient evidence to recommend additional supplementation or screening beyond current national guidelines for the prevention of osteomalacia, falls, and fractures in older adults (i.e., those aged >50 years).

These recommendations may change as vitamin D research continues to evolve. Therefore, the Workgroup currently plans to continue meeting periodically to review the medical literature on this topic.

Introduction

Vitamin D is an essential fat-soluble vitamin best known for its role in promoting bone health through the maintenance of adequate calcium and phosphorus levels, which are required for proper bone metabolism. Vitamin D deficiency is known to cause bone disorders, including rickets in children and osteomalacia in adults. In 2011, the Institute of Medicine published updated vitamin D recommendations that provide vitamin D cut points for sufficiency and deficiency (Table 1), as well as updated Dietary Reference Intakes (DRIs).¹ These DRIs represent the daily dietary intake that is considered sufficient to maintain bone health and normal calcium metabolism in healthy persons, assuming minimal sunlight exposure.

Table 1. Serum 25-hydroxyvitamin D (25[OH]D) Image: Comparison of the second secon
Concentration Cut Points and Associated Health
Impacts — Institute of Medicine, 2011 ¹

Serum Level		Health Impacts in Healthy	
nmol/L	ng/mL	Persons	
<30	<12	Associated with vitamin D deficiency, which can lead to rickets in infants and children and osteomalacia in adults	
30 to <50	12 to <20	Generally considered inadequate for bone and overall health in healthy persons	
≥50	≥20	Generally considered adequate for bone and overall health in healthy persons	
>125	>50	Emerging evidence links potential adverse effects to such high levels	

Many professional organizations and medical bodies have also published vitamin D supplementation and screening recommendations, primarily to ensure bone health in selected populations.^{2–10}

In August 2017, the Alaska Section of Epidemiology published a *Recommendations and Reports* that provided a review of the sources of vitamin D, the roles of vitamin D in the body, the current screening and supplementation recommendations available from selected professional organizations and medical bodies, and the available Alaska-specific vitamin D research findings.¹¹

One of the key research findings highlighted in the report is that during 2001–2010, Alaska Native children aged <10 years living in Alaska experienced almost double the rate of rickets-associated hospitalization compared to the U.S. pediatric population aged <10 years (2.23 vs. 1.23 cases per 100,000 children, respectively).¹² Another key finding from the report is that consumption of vitamin D-rich traditional foods (e.g., oily fish and marine mammals) appears to be decreasing in younger Alaska Native people.

Because rickets is not a reportable condition in Alaska, it is difficult to ascertain statewide rates and characteristics of cases not identified in scientific studies. Moreover, rickets in non-Native children has not been well studied in Alaska; only one published study has reported documented rickets in non-Native Alaska children (in three black children during the 1990s).¹³ Fortunately, more work has been done to characterize the incidence and demographic characteristics of rickets cases in Canada. For example, one broad study found that during July 2002 through June 2004, the incidence of vitamin Ddeficiency rickets in Canada was 2.9 cases per 100,000 children.¹⁴ Of the 103 cases in this study for whom data on skin color were available, 92 (89%) were intermediate or darker skinned, and 11 (10%) were fair skinned. In this study, rickets was also identified most frequently in children who were breast-fed and living in the north (i.e., Yukon Territory, Northwest Territories, and Nunavut). Moreover, the following maternal characteristics were identified as contributing factors to childhood rickets: darker skin color, lack of sun exposure, and inadequate vitamin D intake or supplementation.14

Prompted by the high rate of rickets among Alaska Native children, decreased dietary vitamin D intake among many Alaska Native people, and the low sunlight exposure in Alaska during much of the year, in November 2017, the Alaska Division of Public Health assembled the Alaska Vitamin D Workgroup, which is comprised of 15 health care providers and vitamin D subject matter experts from Alaska, Washington, and Canada. The goals of the Workgroup are to a) review and evaluate the scientific evidence regarding the roles of vitamin D in human health, b) review Alaska's unique risk factors for vitamin D deficiency, rickets, and osteomalacia, and c) determine if Alaska-specific vitamin D supplementation or screening recommendations are warranted to prevent rickets and other conditions, such as osteomalacia, that have been demonstrated to be caused by vitamin D deficiency. The Workgroup's recommendations are provided in this report.

Methods

To determine if Alaska-specific vitamin D guidelines are warranted, the Alaska Vitamin D Workgroup conducted an extensive review of the medical literature on vitamin D, with particular focus on large randomized controlled trials (RCTs) and metaanalyses, as well as studies specific to Alaska and other Arctic regions. Moreover, the Workgroup the current national vitamin evaluated D supplementation and screening guidelines, and assessed the safety and efficacy of increased vitamin D supplementation beyond the current national guidelines.

Two in-person meetings were held. The first meeting (December 2017) focused on the current scientific literature surrounding vitamin D deficiency and the available supplementation and screening guidelines for vitamin D from professional organizations and medical bodies. The second meeting (February 2018) focused on reviewing the vitamin D literature and supplementation and screening recommendations for the prevention of rickets in infants and pregnant women and the prevention of osteomalacia, falls, and fractures in adults aged >50 years.

Proposed Alaska-specific vitamin D recommendations for supplementation and screening of infants and pregnant women were drafted and subsequently presented at internal medicine and pediatric grand rounds in Anchorage for discussion and comment by the medical community. Based on feedback from these presentations, the vitamin D recommendations were revised by the Workgroup and incorporated into the current document.

Findings and Recommendations

Infants

Current Supplementation Guidelines

Current guidelines from the American Academy of Pediatrics (AAP) recommend that all newborns receive 400 IU/day of vitamin D starting in the first few days of life.³ This includes entirely or partially breastfed infants, and non-breastfed infants who consume <1 L/day of formula. While AAP notes that children at risk for vitamin D deficiency such as those with darker skin, fat malabsorption, or obesity might require higher doses, they do not offer a suggested vitamin D dose for higher-risk children. AAP advises against routine screening of healthy children, including those considered to have certain risk factors for vitamin D deficiency (i.e., dark skin and obesity) because the available scientific evidence has not demonstrated a beneficial correlation between screening and improving skeletal health within these demographics.⁴ However, AAP does recommend screening for vitamin D deficiency in children and adolescents with conditions associated with reduced bone mass or recurrent low-impact fractures.

The Canadian Paediatric Society (CPS), a scientific body representing a population with similar risk factors for vitamin D deficiency as Alaska, developed recommendations for vitamin D supplementation in 2007.¹⁵ Along with AAP, they recommend that all infants should receive 400 IU/day starting in the first few days of life regardless of breastfeeding status. However, CPS recommends that infants living above 55° north latitude, and those living in the 40-55° north latitude range with additional risk factors for vitamin D deficiency should receive 800 IU/day during the winter months (October-April).15 CPS has not issued recommendations for universal screening of vitamin D. These recommendations are presently under revision including consideration for at-risk Indigenous infants to supplement with 800 IU/day year-round, rather than just during the winter months, to simplify guidelines (James Irvine, MD, personal the communication).

Supplementation Safety and Effect on Serum Concentrations

The National Academy of Medicine (NAM; formerly the Institute of Medicine) tolerable upper intake levels for infants aged 0-6 and 6-12 months are 1,000 and 1,500 IU/day, respectively. These levels were established based on studies showing a lack of adverse health effects, and limited evidence of an additional protective influence above 1,800 IU/day.1 A more recent study in 132 infants demonstrated that supplementing infants with 400, 800, 1,200, and 1,600 IU/day maintained levels >50 nmol/L (an adequate vitamin D level as defined by NAM) at 3 months and sustained this in 98% of infants at 12 months.¹⁶ No adverse health outcomes were observed in any of the infants during follow-up.14 Evidence from additional studies has also shown that doses up to 1,600 IU/day are not associated with adverse outcomes, like hypercalcemia or hypercalciuria in infants.^{17,18}

A University of Iowa randomized dose-response trial with exclusively breast-fed infants conducted during the winter months at 41° N latitude compared supplementation with 200, 400, 600, and 800 IU/day starting at 1 month of age. At enrollment, 72% of infants had levels <50 nmol/L. Supplementation with 800 IU/day was the only dosage that increased and

maintained serum levels to >50 nmol/L in all infants by 5.5 months. With supplementation of 400 IU/day, 14% of infants were <50 nmol/L and 5% were <30 nmol/L at 5.5 months.¹⁸ It was suspected that the failure of some of the infants to reach vitamin D sufficiency while receiving supplementation may have been due to a vitamin D deficient state upon entering the trial. Several other studies have depicted similar results with 8%-30% of infants remaining vitamin D insufficient despite supplementation with 400 IU/day.19-21 Moreover, multiple case studies from Canada demonstrated that symptomatic vitamin D deficiency can occur in high-risk infants supplemented with 400 IU/day because of severe maternal vitamin D deficiency and lack of supplementation during pregnancy.^{22,23}

Workgroup Supplementation Recommendations

In sum, a) while supplementing infants with 400 IU/day of vitamin D is adequate to prevent rickets in infants born with sufficient vitamin D levels, 400 IU/day appears to be inadequate to prevent rickets in some infants born to severely deficient mothers; b) supplementing infants with 800 IU/day of vitamin D appears to be more effective at increasing infant vitamin D levels from insufficiency to sufficiency than supplementing with lower amounts; and c) supplementing infants with 800 IU/day appears to be safe. Therefore, for the prevention of rickets, the Alaska Vitamin D Workgroup recommends that clinicians consider prescribing 800 IU/day of vitamin D to infants who are exclusively or partially breastfed (Table 2).

The Workgroup further recommends that clinicians continue prescribing 400 IU/day of vitamin D to all infants who are exclusively formula-fed *in addition to* the 400 IU/liter of vitamin D contained in their formula (Table 2).

Finally, while not generally recommended, some women choose to supplement with \geq 4,000 IU/day during lactation. Such high daily doses of vitamin D result in increased concentrations of vitamin D in the breastmilk.^{24–26} Therefore, consideration should be given to recommending 400 IU/day instead of 800 IU/day for exclusively or partially breast-fed infants of mothers who are taking \geq 4,000 IU/day of vitamin D while breastfeeding (Table 2).

Workgroup Screening Recommendations

Due to the absence of evidence supporting the role of screening healthy infants for vitamin D deficiency in preventing rickets and the potential high costs involved, the Alaska Vitamin D Workgroup does not recommend universal screening for vitamin D deficiency among infants to prevent rickets. Clinical discretion should be used to determine when to screen individual children for vitamin D deficiency based on their particular risk profile (e.g., children at increased risk of bone fragility and those with recurrent and lowimpact fractures).

Pregnant Women

Newborn vitamin D levels are highly dependent on maternal vitamin D levels, and so infants born to mothers with vitamin D deficiency are also at elevated risk for deficiency.^{27–29} Therefore, a complementary approach to preventing rickets in infancy is preventing vitamin D deficiency in pregnant women.

Alaska-specific Findings

Congenital rickets, defined as the presence of rickets in the first month of life, is linked to maternal vitamin D deficiency during pregnancy.^{30,31} A study of women of childbearing age from the Yukon-Kuskokwim (YK) Delta region demonstrated a decline in serum 25hydroxyvitamin D (25[OH]D) concentrations from the 1980s to the 2010s, which was accompanied by a decline in traditional marine food intake in these women during the 1960s through the 1990s.³² The transition away from a traditional diet in women may have contributed to the high incidence of rickets in Alaska Native children since the 1990s, including several infants with congenital rickets.^{12,33} In addition, two studies of vitamin D levels in pregnant Alaska Native women from the Southwest and the YK Delta regions showed that 28%-60% of maternal blood samples were <50 nmol/L, 91% of cord blood samples at delivery were <50 nmol/L, and 53% of those same cord blood samples were <35 nmol/L.34 Additional studies have shown concerning rates of vitamin D deficiency and insufficiency in other populations during pregnancy.^{29, 35–38}

During May 2016 through January 2018, 211 pregnant women at YK Delta Regional Hospital were screened for vitamin D deficiency at two time points during their pregnancy (preferably during the first and third trimester). Of these, 29 (14%) were vitamin D deficient (i.e., <30 nmol/L) and 112 (53%) were vitamin D insufficient (i.e., <50 nmol/L) at the time of their first screening.³⁹

Current Supplementation Guidelines

NAM and the American College of Obstetricians and Gynecologists (ACOG) have both issued national

vitamin D supplementation guidelines for pregnant women. The NAM recommendation is for all pregnant women to consume 600 IU/day from dietary intake or supplementation with a tolerable upper intake level of 4,000 IU/day.¹ ACOG states that recommendations for routine vitamin D supplementation during pregnancy beyond that contained in a prenatal vitamin, which is typically 400 IU of vitamin D, should await more evidence from clinical trials.⁵ However, ACOG also states that 1,000-2,000 IU/day of vitamin D is considered safe when vitamin D deficiency is identified in pregnant women.5 In addition, they state that evidence suggests that vitamin D deficiency is common during pregnancy, especially among highrisk groups, including women with limited sun exposure (e.g., those who live in cold climates, reside in northern latitudes, or wear sun and winter protective clothing) and ethnic minorities (especially those with darker skin). Most pregnant women in Alaska would fall into one of these high-risk groups. Lastly, a number of additional studies have shown doses up to 5,000 IU/day to be safe in pregnant women.⁴⁰⁻⁴³

Some variation exists regarding vitamin D intake recommendations for pregnant women in other countries. In Canada, CPS recommends that administering up to 2,000 IU/day during the winter months should be considered for pregnant women.¹⁵ The Canadian version of ACOG, the Society of Obstetricians and Gynecologists of Canada, has not issued specific recommendations for a vitamin D supplementation dose, but maintains that all Canadian women should take a vitamin D supplement if they consume insufficient dietary vitamin D, have darker skin pigmentation, or cover their skin.⁴¹ In Australia and New Zealand, the obstetric clinical guidelines indicate that testing should be considered for all pregnant women who are at increased risk of vitamin D deficiency (i.e., those with reduced sunlight skin exposure, those who use sunscreen on a regular basis, those with dark skin, those with a BMI >30, and mothers of infants with rickets). They recommend daily supplementation with 400 IU if the vitamin D level is >50nmol/L, 1,000 IU if the level is 30-49 nmol/L, and 2,000 IU if level is <30 nmol/L.45,46 Additionally, the Royal College of Obstetricians and Gynaecologists (RCOG) recommends 400 IU for all pregnant women and 1,000 IU for at-risk women (e.g., those with darker skin pigmentation or reduced exposure to sunlight).⁴⁷

Supplementation Safety and Effect on Serum Concentrations

A number of recent studies offer additional evidence in support of maternal supplementation during

pregnancy. For example, prenatal vitamin D supplementation studies show increased maternal vitamin D concentrations at term in mothers supplemented with vitamin D compared to placebo or groups.40,48 Moreover, control vitamin D supplementation during pregnancy contributes to increased umbilical cord and neonatal vitamin D levels.^{49,50} Prenatal vitamin D supplementation has also been associated with higher birthweight and decreased risk of small for gestational age, and supplementation with doses of 2000 IU/day or less during pregnancy may reduce fetal or neonatal mortality.⁵¹ Lastly, maternal vitamin D levels have been shown to decrease during pregnancy in women not receiving vitamin D supplementation.^{52, 53}

Multiple studies indicate that current prenatal vitamin D supplementation guidelines in the United States may not be adequate to ensure sufficient vitamin D levels in all pregnant women.^{29,54,55} One study of motherinfant pairs found that 50% (20/40) of the women were vitamin D deficient (<30 nmol/L) at term, despite 70% reporting regularly taking prenatal vitamins with 400 IU/day of vitamin D.²⁹ Similarly, another study found 32% (147/467) of women to be vitamin D insufficient (<50 nmol/L) in late pregnancy despite 74% of those women taking vitamin D supplements, the majority of which were prenatal vitamins containing 400 IU/day.54 In a study comparing supplementation of 400 IU/day to 4,400 IU/day in 806 pregnant women, the mean vitamin D concentration in the cord blood of women taking 400 IU/day throughout their pregnancy was insufficient (19.2 ng/mL or 47.9 nmol/L), and the mean vitamin D concentration in the cord blood of women taking 4,400 IU throughout their pregnancy was sufficient (28.0 ng/mL or 69.9 nmol/L).55 Supplementation with 400 IU/day only increased vitamin D levels in women by 4.2 ng/mL (10.5 nmol/L) between baseline and the third trimester, which is inadequate to bring women out of severe vitamin D deficiency.55

Finally, several studies on the interrelationship between the vitamin D status of the mother and the breastfeeding infant have demonstrated that, while not generally recommended for breastfeeding women, 4,000-6,400 IU/day of vitamin D may ensure adequate status of both the mother and the nursing infant.^{24–26} In one study, infants of mothers receiving 4,000 IU/day exhibited increases in vitamin D concentrations from 13.4 ± 3.3 to 30.8 ± 5.0 ng/mL (33.4 ± 8.2 to $76.9 \pm$ 12.5 nmol/L), which is well above NAM's vitamin D sufficiency threshold (i.e., >20 ng/mL or 49.9 nmol/L).²⁶

Workgroup Supplementation Recommendations

In sum, a) congenital rickets is associated with maternal vitamin D deficiency during pregnancy; b) the 400 IU/day of vitamin D typically contained in prenatal multivitamins does not appear to be enough to ensure sufficient vitamin D levels among all women throughout their pregnancy; c) when vitamin D insufficiency or deficiency is identified or suspected in pregnant women, supplementation with 1,000-2,000 IU/day is recommended by multiple professional organizations nationally and internationally; and d) supplementing pregnant women with 1,000-2,000 IU/day of vitamin D has shown no adverse health outcomes in multiple clinical trials,^{39,46} and is well below the NAM tolerable upper limit for pregnant women (4,000 IU/day). Therefore, the Alaska Vitamin D Workgroup recommends that clinicians consider supplementing pregnant women living in Alaska with 1,000 IU/day, in addition to the daily prenatal vitamin containing 400 IU of vitamin D, for a total of 1,400 IU/day (Table 2).

Workgroup Screening Recommendations

At this time, the Alaska Vitamin D Workgroup does not recommend universal screening for vitamin D deficiency among pregnant women in order to prevent rickets in their children because of insufficient evidence of the cost–effectiveness in reducing the incidence of rickets. Clinical discretion should be used to determine when to screen individual pregnant women for vitamin D deficiency based on their particular risk profile.

Older Adults

Supplementation Safety and Effect on Serum Concentrations

Osteomalacia is a disorder of decreased bone mineralization that occurs in adults; it is most often caused by severe vitamin D deficiency.⁵⁶ As people age, their risk for osteomalacia, and subsequent falls and fractures, increases.⁵⁶ However, in 2018, the U.S. Services Task Force (USPSTF) Preventative recommended against routine vitamin D supplementation to prevent falls in communitydwelling adults aged ≥ 65 years.⁵⁷ This was based on inconsistent findings from five clinical trials, which included one trial reporting increased risks of both falls and fractures among people who supplemented with vitamin D.58 In a simultaneously published report, the USPSTF concluded that the current evidence was insufficient to assess the balance of the benefits and harms of vitamin D and calcium supplementation, alone or combined, for the primary prevention of fractures in asymptomatic, communitydwelling men and premenopausal women.⁵⁸ They also recommended against daily supplementation with \leq 400 IU of vitamin D and \leq 1,000 mg of calcium for the primary prevention of fractures in postmenopausal women. They concluded that there is still insufficient evidence to assess the balance of benefits and harms of daily supplementation with >400 IU/day of vitamin D for the prevention of fractures in communitydwelling post-menopausal women.⁵⁹

In Alaska specifically, older Alaska Native people tend to have higher vitamin D levels than younger Alaska Native people because they tend to consume more traditional foods.^{29,60–63} For example, one study of Alaska Yup'ik people demonstrated that despite low levels of sun exposure, circulating concentrations of 25(OH)D were within the recommended optimal range.⁶⁰ The authors suggested that genetic adaptations and the high vitamin D content found in traditional foods may have helped maintain adequate concentrations of vitamin D. Further evidence for this comes from studies that demonstrate positive associations between biomarkers of a traditional marine diet and increased vitamin D concentrations, with the highest levels found in older age groups.^{61–63}

Recommendations for the age at which older adults should start increasing their vitamin D intake varies depending on the organization. The NAM recommends 800 IU/day for all persons aged \geq 70 years,¹ while professional bodies like the National Osteoporosis Foundation and Osteoporosis Canada recommend increasing supplementation up to 1,000 IU/day starting at 50 years of age.^{8,10}

Workgroup Supplementation and Screening Recommendations

In sum, a) the current evidence is insufficient to assess the balance of the benefits and harms of vitamin D and calcium supplementation, alone or combined, for the primary prevention of fractures in asymptomatic community-dwelling men and premenopausal women, and b) current recommendations already take into account the vulnerability of older adults to increased bone loss and subsequent falls and fractures by increasing the recommended intake of vitamin D from 600 IU/day to 800–1,000 IU/day.^{1,10} Therefore, the Alaska Vitamin D Workgroup does not recommend vitamin D supplementation or screening for older adults beyond what is currently recommended by NAM and other professional organizations.

Conclusion

The Alaska Vitamin D Workgroup concludes that the bulk of the available scientific evidence appears to support increased vitamin D supplementation, beyond the current national recommendations, in Alaska infants and pregnant women for the prevention of childhood rickets.

The Workgroup also concludes that a) there is insufficient cost-effectiveness evidence to recommend universal screening of infants or pregnant women for vitamin D deficiency for the prevention of rickets, and b) there is insufficient evidence to recommend additional supplementation or screening beyond current national guidelines for the prevention of osteomalacia, falls, and fractures in older adults (i.e., those aged >50 years).

The recommendations proposed here may change as vitamin D research continues to evolve. With this in mind, the Alaska Vitamin D Workgroup currently plans to continue meeting periodically to review the medical literature on this topic.

Finally, it is important to note that Alaska Medicaid will cover vitamin D supplementation of up to 800 IU/d for infants and 1,000 IU/d for pregnant women (in addition to the daily multivitamin).

Population		Dietary Intake/Supplementation	Screening
Newborns and Infants (0–12 months)*	Exclusively or partially breast-fed infants	Consider supplementation with 800 IU/day [†]	Not routinely recommended
	Exclusively formula-fed infants	Consider supplementation with 400 IU/day in addition to the 400 IU/liter contained in the formula	
Pregnant Women*		Consider supplementation with 1,000 IU/day in addition to a daily prenatal vitamin containing 400 IU/day (not to exceed 4,000 IU/day)	Not routinely recommended
Children and Adults (1–70 years)		Follow National Academy of Medicine intake recommendation of 600 IU/day (through diet and/or supplementation)	Not routinely recommended
Elderly (>70 years)		Follow National Academy of Medicine intake recommendation of 800 IU/day (through diet and/or supplementation)	Not routinely recommended

*The increased supplementation recommendations for infants and pregnant women are for the prevention of childhood rickets in Alaska.

†Decrease infant supplementation to 400 IU/day if their mother is supplementing with \geq 4,000 *IU/day of vitamin D while breastfeeding.*

References

- 1. IOM (Institute of Medicine). 2011. Dietary reference intakes for calcium and vitamin D. Washington, DC: The National Academies Press.
- LeBlanc ES, Zakher B, Daeges M, et al. Screening for vitamin d deficiency: A systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2015;162(2):109–22.
- 3. Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Am Acad Pediatr* 2008;122:1142–52.
- Perrine CG, Sharma AJ, Jefferds MED, et al. Adherence to vitamin D recommendations among US infants. *Am Acad Pediatr* 2010;125(4):627– 32.
- Vitamin D: screening and supplementation during pregnancy. Committee Opinion No. 495. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2011;118:197–8.
- 6. American Geriatrics recommendations abstracted from the American Geriatrics Society Consensus Statement on vitamin D for prevention of falls and their consequences. *J Am Geriatr Soc* 2014;62(1):147–52.
- 7. Vitamin D. International Osteoporosis Foundation. Available at: https://www.iofbonehealth.org/osteoporosismusculoskeletaldisorders/osteoporosis/prevention/vitamin-d.
- Vitamin D. Osteoporosis Canada. 2017. Available at: <u>https://osteoporosis.ca/bone-healthosteoporosis/calcium-and-vitamin-d/vitamin-d/.</u>
- 9. Vitamin D and calcium: updated dietary reference intakes. Health Canada. 2011. Available at: <u>https://www.canada.ca/en/health-</u> <u>canada/services/food-nutrition/healthy-</u> <u>eating/vitamins-minerals/vitamin-calcium-</u> <u>updated-dietary-reference-intakes-nutrition.html</u>
- 10. Calcium/Vitamin D. National Osteoporosis Foundation. 2018. Available at: <u>https://www.nof.org/patients/treatment/calciumvi</u>tamin-d/
- 11. Alaska Epidemiology *Recommendations and Reports.* "A Brief Overview on Vitamin D for

Alaska Healthcare Providers." Vo. 19, No. 3, August 17, 2017. Available at: <u>http://www.epi.alaska.gov/bulletins/docs/rr2017</u>_3.pdf

- 12. Singleton R, Lescher R, Gessner BD, et al. Rickets and vitamin D deficiency in Alaska Native children. *J Pediatr Endocrinol Metab* 2015;28(0):815–23.
- 13.Gessner BD, DeSchweinitz E, Petterson KM, Lewandowski C. Nutritional rickets among breast-fed Black and Alaska Native children. *Alaska Med* 1997;39(3):72–4.
- 14. Ward LM, Gaboury I, Ladhani M, Zlotkin S. Vitamin D-deficiency rickets among children in Canada. *CMAJ* 2007;177(2):161–6.
- 15. Godel JC. Vitamin D supplementation: Recommendations for Canadian mothers and infants. *Paediatr Child Health* 2007;12(7):583–9.
- 16. Gallo S, Comeau K, Vanstone C, et al. Effect of different dosages of oral vitamin D supplementation on vitamin D status in healthy, breastfed infants. *JAMA* 2013;309(17):1785–92.
- 17. Holmlund-Suila E, Viljakainen H, Hytinantti T, et al. High-dose vitamin D intervention in infants Effects on vitamin D status, calcium homeostasis, and bone strength. *J Clin Endocrinol Metab* 2012;97(11):4139–47.
- 18.Ziegler EE, Nelson SE, Jeter JM. Vitamin D supplementation of breastfed infants: a randomized dose-response trial. *Pediatr Res* 2014;76(2):177–83.
- 19. Aghajafari F, Field CJ, Weinberg AR, et al. Both mother and infant require a vitamin D supplement to ensure that infants' vitamin D status meets current guidelines. *Nutrients* 2018;10(429).
- 20. Saadi HF, Dawodu A, Afandi B, et al. Effect of combined maternal and infant vitamin D supplementation on vitamin D status of exclusively breastfed infants. *Matern Child Nutr* 2009;5(1):25–32.
- 21. Specker BL, Ho ML, Oestreich A, et al. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 1992;120(5):733– 9.

- 22. Gross ML, Tenenbein M, Sellers EAC. Severe vitamin D deficiency in 6 Canadian First Nation formula-fed infants. *Int J Circumpolar Health* 2013;72.
- 23. Ward LM, Frcpc M, Ladhani M, et al. Severe vitamin D deficiency: A persistent yet preventable problem among Canadian youth CASE 1. *Paediatr Child Health* 2017;22(1):43–4.
- 24. Hollis BW, Wagner CL. Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. *Am J Clin Nutr* 2004;80(6 Suppl):1752S–8S.
- 25. Oberhelman SS, Meekins ME, Fischer PR, et al. Maternal vitamin D supplementation to improve the vitamin D status of breast-fed infants: A randomized controlled trial. *Mayo Clin Proc* 2013;88(12):1378–87.
- 26. Hollis BW, Wagner CL, Howard CR, et al. Maternal versus infant vitamin D supplementation during lactation: a randomized controlled trial. *Pediatrics* 2015;136(4):625–34.
- 27. Hillman LS, Haddad JG. Human perinatal vitamin D metabolism. I. 25-Hydroxyvitamin D in maternal and cord blood. *J Pediatr*. 1974;84(5):742–9.
- 28. Hollis BW, Pittard WB. Evaluation of the total fetomaternal vitamin D relationships at term: evidence for racial differences. *J Clin Endocrinol Metab* 1984;59(4):652–7.
- 29. Lee JM, Smith JR, Philipp BL, et al. Vitamin D deficiency in a healthy group of mothers and newborn infants. *Clin Pediatr* 2007;46(1):42–4.
- 30. Munns CF, Simm PJ, Rodda CP, et al. Incidence of vitamin D deficiency rickets among Australian children: An Australian Paediatric Surveillance Unit study. *Med J Aust* 2012;196(7):466–8.
- 31. Fiscaletti M, Stewart P, Munns C. The importance of vitamin D in maternal and child health: a global perspective. *Public Health Rev* 2017;38(19).
- 32. O'Brien DM, Thummel KE, Bulkow LR, et al. Declines in traditional marine food intake and vitamin D levels from the 1960s to present in

young Alaska Native women. *Public Health Nutr* 2016;1–8.

- 33. Gessner BD, Plotnik J, Muth PT. 25hydroxyvitamin D levels among healthy children in Alaska. *J Pediatr* 2003;143(4):434–7.
- 34. Alaska Epidemiology Bulletin. "Vitamin D Deficiency in Prenatal Alaska Native Women" No. 27, November 1, 2016. Available at: <u>http://www.epi.alaska.gov/bulletins/docs/b2016</u> 27.pdf
- 35.Looker AC, Johnson CL, Lacher DA, et al. Vitamin D status: United States, 2001–2006. NCHS data brief, no 59. Hyattsville, MD: NCHS. 2011.
- 36. Saraf R, Morton SMB, Camargo CA, et al. Global summary of maternal and newborn vitamin D status – a systematic review. *Matern Child Nutr* 2016;12(4):647–68.
- 37.Lehotay DC, Smith P, Krahn J, et al. Vitamin D levels and relative insufficiency in Saskatchewan. *Clin Biochem* 2013;46(15):1489–92.
- 38. Bodnar LM, Simhan HN, Powers RW, et al. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr* 2007;137(2):447–52.
- 39. Singleton, R, et al. Yukon Delta Regional Hospital; unpublished data, prenatal vitamin D supplementation. 2018.
- 40. Roth DE, Leung M, Mesfin E, et al. Vitamin D supplementation during pregnancy: state of the evidence from a systematic review of randomised trials. *BMJ* 2017;359.
- 41. Roth DE, Al Mahmud A, Raqib R, et al. Randomized placebo-controlled trial of high-dose prenatal third-trimester vitamin D3 supplementation in Bangladesh: the AViDD trial. *Nutr J* 2013;12(47).
- 42. Dawodu A, Saadi HF, Bekdache G, et al. Randomized controlled trial (RCT) of vitamin D supplementation in pregnancy in a population with endemic vitamin D deficiency. *J Clin Endocrinol Metab* 2013;98(6):2337–46.
- 43. Hollis BW, Johnson D, Hulsey TC, et al. Vitamin D supplementation during pregnancy: double-

blind, randomized clinical trial of safety and effectiveness. J Bone Miner Res 2011;26(10):2341–57.

- 44.O'Connor DL, Blake J, Bell R, et al. Canadian consensus on female nutrition: adolescence, reproduction, menopause, and beyond. *J Obstet Gynaecol Canada* 2016;38(6):508–54.
- 45. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College Statement and Guideline C-Obs 25. Vitamin and mineral supplementation and pregnancy. 2015. Available at: https://www.ranzcog.edu.au/RANZCOG SITE/ media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20 and%20guidelines/Clinical-Obstetrics/Vitaminand-mineral-supplementation-in-pregnancy-(C-Obs-25)-Review-Nov-2014,-Amended-May-2015.pdf?ext=.pdf [accessed 08.02.18].
- 46. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College Statement and Guideline C-Obs 03b. Routine antenatal assessment in the absence of pregnancy complications. 2016. Available at: <u>https://www.ranzcog.edu.au/college-statementsguidelines.html</u> [accessed 05.10.18].
- 47. Royal College of Obstetricians and Gynaecologists. Vitamin D in pregnancy. Scientific Impact Paper No. 43. 2014. Available at: <u>https://www.rcog.org.uk/en/guidelinesresearch-services/guidelines/sip43/</u> [accessed 05.10.18].
- 48. De-regil L, Palacios C, Ansary A, et al. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2016;(1).
- 49. Grant CC, Stewart AW, Scragg R, et al. Vitamin D during pregnancy and infancy and infant serum 25-hydroxyvitamin D concentration. *Pediatrics* 2014;133(1):e143–53.
- 50. Sablok A, Batra A, Thariani K, et al. Supplementation of vitamin D in pregnancy and its correlation with feto-maternal outcome. *Clin Endocrinol* 2015;83(4):536–41.
- 51.Bi WG, Nuyt AM, Weiler H, Leduc L, Santamaria C, Wei SQ. Association Between Vitamin D Supplementation During Pregnancy and Offspring Growth, Morbidity, and Mortality: A

Systematic Review and Meta-analysis. *JAMA Pediatr* 2018;172(7):635–45.

- 52. Fernández-Alonso AM, Dionis-Sánchez EC, Chedraui P, et al. First-trimester maternal serum 25-hydroxyvitamin D3status and pregnancy outcome. *Int J Gynecol Obstet* 2012;116(1):6–9.
- 53. Hossain N, Khanani R, Hussain-Kanani F, et al. High prevalence of vitamin D deficiency in Pakistani mothers and their newborns. *Int J Gynecol Obstet* 2011;112(3):229–33.
- 54. Zhang JY, Lucey AJ, Horgan R, et al. Impact of pregnancy on vitamin D status: A longitudinal study. *Br J Nutr* 2014;112(7):1081–87.
- 55. Kramer CK, Ye C, Swaminathan B, et al. The persistence of maternal vitamin D deficiency and insufficiency during pregnancy and lactation irrespective of season and supplementation. *Clin Endocrinol* 2016;84(5):680–6.
- 56. Sunyecz JA. The use of calcium and vitamin D in the management of osteoporosis. *Ther Clin Risk Manag* 2008;4(4):827–36.
- 57. US Preventive Services Task Force. Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults US Preventive Services Task Force Recommendation Statement. *JAMA* 2018;319(15):1592–99.
- 58. US Preventive Services Task Force. Interventions to Prevent Falls in Community-Dwelling Older Adults US Preventive Services Task Force Recommendation Statement. JAMA 2018;319(16):1696–1704.
- 59. Sanders KM, Stuart AL, Williamson EJ, et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled Trial. *JAMA* 2010;303(18):1815–22.
- 60. Aslibekyan S, Vaughan LK, Wiener HW, et al. Linkage and association analysis of circulating vitamin D and parathyroid hormone identifies novel loci in Alaska Native Yup'ik people. *Genes Nutr* 2016;11(23).
- 61.Frost JT, Hill L. Vitamin D deficiency in a nonrandom sample of Southeast Alaska Natives. *J Am Diet Assoc* 2008;108(9):1508–11.

- 62. Luick B, Bersamin A, Stern JS. Locally harvested foods support serum 25-hydroxyvitamin D sufficiency in an indigenous population of Western Alaska. *Int J Circumpolar Health* 2014;73:22732.
- 63. Fohner AE, Wang Z, Yracheta J, et al. Genetics, diet, and season are associated with serum 25hydroxycholecalciferol concentration in a Yup'ik study population from Southwestern Alaska. *J Nutr* 2015;146:318–25.