



Vitamin D screening variations in children and adolescents: Who should be screened?☆

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ABSTRACT

Problem: No consensus on vitamin D deficiency (VDD) screening in children and adolescents exists. Early VDD detection can improve the health of children. VDD can cause bone mineralization diseases, such as rickets in children. The purpose of this review is to determine existing VDD screening recommendations or clinical practice guidelines in children and adolescents.

Eligibility criteria: Inclusion criteria were VDD screening 'guideline', 'clinical practice guideline', and 'recommendations' for children and adolescents in English, published 2001–2018.

Results: Eight current guidelines addressed VDD screening recommendations with the common recommendation results endorsing screening only for VDD in at-risk children and adolescents.

Conclusions: There is insufficient evidence for pediatric healthcare providers to recommend which VDD risk factors should be utilized for screening in children and adolescents.

Implications: Further studies should focus on developing a validated VDD screening tool for children and adolescents based on risk factors.

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Introduction

Vitamin D's effect on the body and interrelationship upon health is a common topic of discussion in research, media and community. To reach peak bone mass in adolescence, one must have the necessary and essential amounts of vitamin D in childhood which directly regulate calcium and phosphorus homeostasis (Saggese et al., 2015). Aside from the large amount of interest, research, and publications, there is disagreement related to vitamin D surrounding the recommended daily allowances (RDA), classifications of normal and abnormal, variations in the assays used to measure serum levels, degree of effect on health, and who should be screened in adults but even less consensus is available for children (LeBlanc, Chou, Zakher, Daeges, & Pappas, 2014).

Organizational guidelines, such as the Institute of Medicine (IOM), focus on the RDA across all age groups (Ross et al., 2011). The RDA for 1–18 years of age range from 200 to 1000 IU/day with the majority recommending 400–600 IU/day (Bouillon, 2017). In relation to diet, one study speculated that it is not possible for children with the

'habitual diet' to meet the RDA by IOM (Black, Walton, Flynn, & Kiely, 2014). Discussion based on RDA focuses only on intake, while children with various backgrounds metabolize and utilize nutrients differently and may need increased vitamin D to have sufficient serum levels that positively supports growth and healthy children and adolescents (Saggese et al., 2015).

The terms sufficient, insufficient and deficient are common terminology for serum vitamin D levels which are measured through the 25-hydroxyvitamin D [25(OH)D]. Sufficient levels vary by organization and range from 25–>100 nmol (10–>40 ng/ml) with 30–50 nmol (20–30 ng/ml) as the most common sufficient levels (Bouillon, 2017). There are calls for consensus for definitions of sufficient and also for the tests that are used to measure vitamin D in order for research to be able to accurately compare and correlate results (Sempos et al., 2018). The research varies on which levels are associated and correlated with abnormal physical findings but 25(OH)D <30 nmol (<12 ng/ml) are at increased risk of rickets or osteomalacia (Sempos et al., 2018).

Physical assessment findings of low 25(OH)D may include swelling of the wrists or ankles, enlarged costochondral joints felt lateral to the nipple line, genu varum/genu valgum, knee pain, frontal bossing, softening of skull bones, hypocalcemia, myopathy, and delayed motor skills (Munns et al., 2006). Low 25(OH)D have been associated with increased risk of fractures, functional limitations, impaired cardiovascular

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health, mental health issues, obesity, impaired glucose metabolism, and decreased bone density but controversy remains related to causation (LeBlanc et al., 2014; Newberry et al., 2014). Severe and prolonged vitamin D deficiency (VDD) can cause bone mineralization diseases, such as rickets in children (Basatemur, Horsfall, Marston, Rait, & Sutcliffe, 2017; Saggese et al., 2015). Additionally, increased severity of chronic diseases exacerbations such as sickle cell and asthma in children have been associated with low 25(OH)D (Bantz, Zhu, & Zheng, 2015; de Oliveira, Vicente, Santos, & Weffort, 2015).

Vitamin D is acquired predominantly through natural sun exposure while only a small amount occurs from vitamin D rich or supplemented foods (Holick, 2012; Saggese et al., 2015). Therefore, issues that affect the methods to acquire, metabolize, or utilize vitamin D create risk factors for low vitamin D. Risk factors include: (1) issues that inhibit or prevent natural sun exposure such as use of sunscreen, dark pigmented skin, and no or small amounts of sunlight including northern geographical location, protective clothing such as veils or coverings, and no or limited outside playtime; (2) diet lacking in vitamin D rich foods; (3) certain medications; and (4) illnesses or disease processes that cause malabsorption, improper utilization, or increased metabolism of vitamin D.

Population based screening is not recommended for VDD for asymptomatic adult populations (>18 years of age) due to lack of current evidence to assess risk and benefits (U.S. Preventive Services Task Force, 2015). Regardless, VDD is becoming a common diagnosis, and rates are rising in adults and children (Huang, Milliron, Davis, & Feldman, 2014). Basatemur et al. (2017) found a fifteen fold increase in the diagnosis of vitamin D deficiency from 2000 to 2014 with an increase in the crude rate from 3.14 to 261 per 100,000 persons in England. Similar studies and reviews are demonstrating consistent findings of increased testing with an increase in subsequent costs of testing (Rockwell, Kraak, Hulver, & Epling, 2018).

Pediatric health care providers (HCPs), such as Pediatric Nurse Practitioners and pediatric nurses, have an important role in the health and well-being of children and adolescents (American Nurse Association, 2015; National Organization of Nurse Practitioner Faculties, 2013). Pediatric HCPs within the comprehensive well exams are routinely reviewing medical and nutritional history, levels of physical activity, amount of sun exposure, and physical exam information that are correlated to VDD. There may be confusion or uncertainty regarding which risk factors are significant for VDD or how many risk factors warrant screening in children and adolescents. The purpose of this integrative review is to determine the existing screening guidelines, clinical practice guidelines, or recommendations for VDD in children and adolescents.

Methods

Searching strategy

This integrative review included electronic and manual sources of non-experimental research, experimental, and quasi-experimental research that used any guidelines or recommendations of vitamin D screening, assessment, or treatment for children and adolescents reviewed through September 2017 and December 2018. The inclusion criteria of the studies included: (1) Publications between 2001 and 2018; (2) Publication in the English language; and (3) vitamin D 'guidelines', 'clinical practice guidelines', or 'recommendations' for screening children and adolescents. The exclusion criteria of the studies included: (1) Systematic reviews; (2) 'Guidelines', 'clinical practice guidelines', or 'recommendations' that did not include screening for children and adolescence; (3) Studies that did not include 'guidelines', 'clinical practice guidelines', or 'recommendations'; and (4) Previous or prior editions/older guidelines, clinical practice guidelines or recommendations that have been updated by the organization.

The seven steps of research synthesis approach developed by Cooper (2010) was the guiding framework for this integrative review. Cooper identifies the process of conducting an integrative review as encompassing the following seven stages: (1) formulating the problem, (2) searching the literature, (3) gathering information from studies, (4) evaluating the quality of studies, (5) analyzing and integrating the outcomes of studies, (6) interpreting the evidence, and (7) presenting the results. The integrative review provides several contributions to the scholarly reviewer, which include identifying gaps in past and current research, identifying the need for future research, bridging between related areas of inquiry, identifying central issues in an area, and identifying whether theoretical or conceptual frameworks were utilized (Cooper, 2010).

According to Cooper (2010), integrative reviews summarize and synthesize information from various empirical research articles that highlight the most relevant issues. Whittemore and Knafelz (2005) mentioned that the inclusion of both experimental and non-experimental research help to fully understand a phenomenon of concern which makes the integrative review one of the broadest types of research reviews.

Data collection

Eligible research articles for this integrative review were obtained through online computer searches utilizing the following databases: CINAHL, PubMed, and SCOPUS. The following keywords were used: "vitamin D" AND "screening" AND "guideline" AND "recommendation" AND "clinical practice" OR "clinical practice guidelines". The authors consulted a librarian regarding search terms and search process for each data base at the beginning of the search. The initial search (2001–2017) identified 310 articles across the three databases and two manually added articles. The authors updated the search through 2018 in January 2019, and 28 articles across the three databases were added for review. After a title and abstract review by the authors, 284 research articles were excluded as irrelevant and/or duplicates. After two of the authors independently reviewed the remaining 56 articles based on inclusion and exclusion criteria, the results revealed eight articles. The detailed process for selection of eligible publications, and the PRISMA steps flow diagram searching strategy is illustrated in Fig. 1.

Results

The results of this integrative review of current vitamin D screening guidelines, clinical practice recommendations, or recommendations for children and adolescents revealed eight articles. Of these results, three were from the United States, three from Europe, and one from Australia/New Zealand and United Arab Emirates/Gulf Cooperation Council respectively (Table 1) (Golden & Abrams, 2014; Grossman et al., 2017; Haq et al., 2016; Holick et al., 2011; Misra et al., 2008; Paxton et al., 2013; Pludowski et al., 2013; Wood & Cheetham, 2016).

All organizations recommend screening those with risk factors but variation occurs on which risk factors should be screened. All of the organizations recommended screening for VDD in children and adolescents who are taking certain medicines or have a malabsorptive syndrome (Table 2). Almost all of the organizations, including the American Academy of Pediatrics (AAP) Committee on Nutrition, the Endocrine Society (ES), the Pediatric Endocrine Society (PES), the European Academy of Paediatrics (EAP), Central Europe Consensus (CEC), the Australia and New Zealand Bone and Mineral Society (ANZBMS) and Osteoporosis Australia, and the National Institute for Health and Care Excellence (NICE) in the United Kingdom recommended screening of those who have lack of or prevention of skin exposure to ultraviolet B, and those who have dark skin such as African-American and Hispanics.

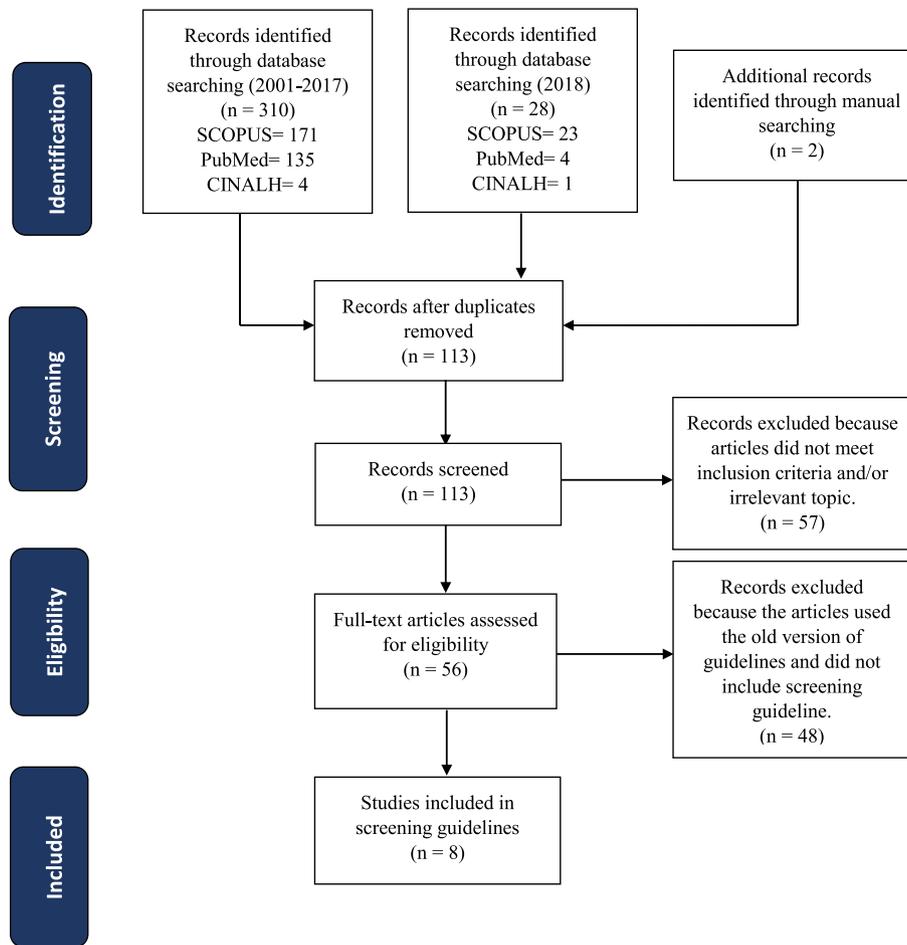


Fig. 1. Diagram illustrating the step search strategy of PRISMA 2009.

In the United States, the ES, AAP and PES agree population-based screening is not feasible or cost-effective and that there is no evidence demonstrating that population based screening for VDD has health outcome benefits (Golden & Abrams, 2014; Holick et al., 2011; Misra et al., 2008). The ES and AAP's clinical practice guidelines for VDD call for only screening individuals at risk and the ES, AAP, and PES organizations generally concur on risk factors for VDD in children and adolescents such as those who take certain medications, those with certain illnesses, diseases, nutritional deficits, weight, and geographical locations that have less sunlight (Golden & Abrams, 2014; Holick et al., 2011). The AAP recommends screening for VDD only in children and adolescents with conditions associated with reduced bone mass, malabsorption or with recurrent low-impact fractures but specifically does not recommend

screening individuals who are obese or darkly pigmented if they are otherwise healthy (Golden & Abrams, 2014). The ES does include similar recommendations to the AAP for screening but also includes children and adults who are obese or with dark pigmented skin such as African-Americans or Hispanics due to how vitamin D is produced, processed, and metabolized (Golden & Abrams, 2014; Holick et al., 2011). Only the PES recommended screening those who have nonspecific symptoms such as poor growth, gross motor delays (Misra et al., 2008).

Outside of the United States, the ANZBMS, the United Arab Emirates and Gulf Cooperation Council (UAE & GCC), NICE, and the CEC's recommendations are similar to the United States guidelines discussing risk factors that warrant screening but recommend screening infants and children with exclusive breastfeeding, children with abnormalities of

Table 1
Integrative literature review summary.

Author (Year)	Organization	Location	Population Focus
Golden and Abrams (2014)	American Academy of Pediatrics (AAP), Nutrition Committee	USA	Children and adolescents
Grossman et al. (2017)	European Academy of Paediatrics (EAP)	Europe	Infants, children and adolescents
Haq, Wimalawansa, Pludowski, and Anouti (2016)	United Arab Emirates and Gulf Cooperation Council (UAE & GCC)	United Arab Emirates	Infants, children, and adults
Holick et al. (2011)	Endocrine Society (ES)	Europe USA	Infants, children, adolescents, adults, and pregnant women.
Misra, Pacaud, Petryk, Collett-Solberg, and Kappy (2008)	Pediatric Endocrine Society (PES)	USA	Infants and children
Pludowski et al. (2013)	Central Europe Consensus (CEC)	Central Europe	General included children and adolescents
Paxton et al. (2013)	Australian and New Zealand Bone and Mineral Society and Osteoporosis Australia (ANZBMS)	Australian and New Zealand	Pregnancy, infants, children, and adolescents
Wood and Cheetham (2016)	National Institute for Health and Care Excellence (NICE)	United Kingdom	Infants, children, pregnant women, and adults

Table 2
Comparison of vitamin D screening recommendations by risk factors.

Risk Factors	Screening Recommendations by Organizations							
	AAP ^a , 2014	ES ^b , 2011	PES ^c , 2008	CEC ^d , 2013	ANZBMS ^e , 2013	NICE ^f , 2016	UAG & GCC ^g , 2016	EAP ^h , 2017
Medications ⁱ	✓	✓	✓	✓	✓	✓	✓	✓
Malabsorptive syndromes ^j	✓	✓	✓	✓	✓	✓	✓	✓
Lack of or prevention of skin exposure to ultraviolet B	✓	✓	✓	✓	✓	✓		✓
Dark skin such as African-American and Hispanic	✓	✓	✓	✓	✓	✓		✓
Eating disorders	✓	✓		✓	✓	✓	✓	
Chronic illness ^k	✓	✓		✓	✓	✓		✓
Reduce bone mass and/or recurrent low-impact fractures	✓		✓	✓	✓	✓		
Rickets, osteomalacia, and osteoporosis	✓	✓	✓			✓	✓	
Hyperparathyroidism	✓	✓		✓		✓	✓	
Genetic conditions ^l	✓	✓	✓			✓		
Diet lacking in vitamin D	✓	✓	✓	✓				✓
Secondary osteoporotic fractures, and history of low energy fractures of different origin	✓			✓		✓		
Patients admitted to hospital due to certain infections				✓		✓	✓	
Infants and children <5 years old with exclusive breastfeeding					✓	✓		
Calcium/phosphate metabolism abnormalities				✓		✓		
Obesity		✓			✓			
Nonspecific symptoms such as poor growth, gross motor delays			✓					
Children on long-term parenteral nutrition								✓
Institutionalized children								✓

^a American Academy of Pediatrics.

^b Endocrine Society.

^c Pediatric Endocrine Society.

^d Central Europe Consensus.

^e Australian and New Zealand Bone and Mineral Society and Osteoporosis Australia.

^f National Institute for Health and Care Excellence.

^g United Arab Emirates and Gulf Cooperation Council Guideline.

^h European Academy of Paediatrics.

ⁱ Medications: glucocorticoids, anticonvulsants, chemotherapy, leuprolide acetate, proton pump inhibitors, SSRI, DMPA.

^j Malabsorptive syndromes: cystic fibrosis, inflammatory bowel disease, Crohn's disease, bariatric surgery, radiation enteritis.

^k Chronic illness: chronic kidney diseases, hepatic failure, granulomatous disorders, cancer, cardiovascular diseases, and some chronic autoimmune diseases, cystic fibrosis, connective tissue disorders (lupus, juvenile idiopathic arthritis, juvenile dermatomyositis, inflammatory bowel disease, celiac disease, chronic renal failure, cerebral palsy, and chronic immobilization).

^l Genetic conditions: osteogenesis imperfecta, idiopathic juvenile osteoporosis, Turner syndrome.

metabolism of calcium or phosphate, or hospitalized with certain infections (Table 2) (Haq et al., 2016; Paxton et al., 2013; Pludowski et al., 2013; Wood & Cheetham, 2016). The ANZBMS consensus statement discusses screening those with decreased or limited sun exposure especially due to coverings such as veils, obesity, or dark skin color (Paxton et al., 2013). NICE and ANZBMS recommend screening for infants, pregnant women, especially those who are dark-skinned or veiled with one or more additional risk factors, and additionally, recommend that breastfed infants of dark-skinned or veiled women be supplemented with vitamin D for the first 12 months of life (Paxton et al., 2013; Wood & Cheetham, 2016). While the EAP also recommends screening institutionalized or children on long-term parental nutrition (Grossman et al., 2017). NICE has the most complete list of screening recommendations of those reviewed (Wood & Cheetham, 2016).

Discussion

Implications for practice

Based on the results of this review, there is a variation of screening recommendations on which risk factors should be screened. The lack of consensus for screening recommendations based on risk factors to identify VDD, especially in children, is a critical gap in the evidence. There is insufficient evidence and guidance for pediatric HCPs to easily decipher which VDD risk factors and thresholds should be utilized for screening because of the lack of consensus in recommendations. Screening vitamin D status in children and adolescents based on risk factors and assessment findings such as certain medication use or specific disease processes may make VDD seem rare or less applicable in general

practice. Providers may not know or are unsure of which recommendations for screening are relevant.

However, VDD risk factors associated with dark skin pigmentation, pediatric obesity, and decreased sun exposure contain a large percentage of the population. An individual could obtain an equivalent to 20,000 IU of vitamin D3 through sun exposure in a bathing suit that results with one minimal erythemal dose (MED) or approximately 3000 IU with sun exposure to only arms and legs at 0.5 MED if they are outside playing on a sunny day (Holick, 2012; Saggese et al., 2015). With less outdoor activity, children and adolescents are missing the best and easiest way to acquire vitamin D.

In the United States, overall obesity rates are 17% for 2–19 year olds while African American and Hispanic populations aged 2–19 years of age have higher obesity percentages (19.5% and 21.9% respectively) (Ogden, Carroll, Fryar, & Flegal, 2015). Jain (2016) reports that 12–19 year old African American children have as low as 2.8% sufficiency rates based solely on age and race. Additionally, VDD have a direct correlation with obesity and inactivity as many children no longer play outside. Providers should be concerned especially for dark skinned populations since our youth are becoming more inactive and obese while thresholds screening are unclear since their bone health is currently being formulized (Golden & Abrams, 2014; Holick et al., 2011).

Conclusion

The integrative review completed determined that there are available for VDD screening guidelines, clinical practice guidelines, or recommendations in children and adolescents within the United States and internationally for HCP's but with some variations on which risk factors that should be screened. The review did find that all articles did

recommend screening those who are taking certain medications and those with malabsorptive syndromes.

VDD screening may improve the health of children with low vitamin levels by allowing early identification. Screening can identify children with VDD prior to the development of adverse health outcomes, assuming thresholds for deficiency can be agreed upon and laboratory testing can be standardized. These steps are imperative strong evidenced based practice to care for the health and wellbeing of children and adolescents. Additionally, further studies should focus on developing a validated vitamin D screening tool for HCPs based on risk factors for children and adolescents to help providers assess the level of risk based on their history and physical exam findings.

Ethical statement

The authors have no ethical or financial disclosures or any conflicts of interest.

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