

# Vitamin D Intake and Cardiometabolic Risk Factors in Adolescents

Carla Moreira, PhD, Pedro Moreira, PhD, Sandra Abreu, PhD, Paula C. Santos, PhD, Isabel Moreira-Silva, PhD, Susana Póvoas, PhD, Jorge Mota, PhD, and Rute Santos, PhD

## Abstract

**Background:** A growing body of research suggests that vitamin D might play an important role in overall health. No data exist on vitamin D intake for the Azorean adolescent population. The purpose of this study was to assess vitamin D intake and investigate a possible association between vitamin D intake and cardiometabolic risk factors in Azorean adolescents.

**Methods:** A cross-sectional school-based study was conducted on 496 adolescents (288 girls) aged 15–18 years from the Azorean Islands, Portugal. Anthropometric measurements (waist circumference and height), blood pressure (systolic), and plasma biomarkers [fasting glucose, insulin, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TGs)] were measured to assess metabolic risk. Homeostasis model assessment (HOMA), TC-to-HDL-C ratio, and waist-to-height ratio were calculated. For each of these variables, a Z-score was computed by age and sex. A metabolic risk score was constructed by summing the Z-scores of all individual risk factors. High risk was considered when the individual had  $\pm 1$  standard deviation (SD) of this score. Vitamin D intake was assessed with a semiquantitative food frequency questionnaire. Participants were classified into quartiles of vitamin D intake. Logistic regression was used to determine odds ratios for high cardiometabolic risk scores after adjusting for total energy intake, pubertal stage, fat mass percentage, and cardiorespiratory fitness.

**Results:** Mean (SD) vitamin D intake was 5.8 (6.5) mg/day, and 9.1% of Azorean adolescents achieved the estimated average requirement of vitamin D (10 mg/day or 400 IU). Logistic regression showed that the odds ratio for a high cardiometabolic risk score was 3.35 [95% confidence interval (CI) 1.28–8.75] for adolescents in the lowest vitamin D intake quartile in comparison with those in the highest vitamin D intake quartile, even after adjustment for confounders.

**Conclusion:** A lower level of vitamin D intake was associated with worse metabolic profile among Azorean adolescents.

## Introduction

Metabolic syndrome comprises a major risk for noncommunicable diseases, including atherogenic dyslipidemia, abdominal obesity, hypertension, insulin resistance, and prothrombotic and proinflammatory states, leading to increased risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM),<sup>1,2</sup> and, therefore, represents a major health risk.<sup>3,4</sup> The risk factors for CVDs, traditionally considered to be adult diseases, have started to appear in children and adolescents.<sup>5</sup> Longitudinal studies have shown that the presence of risk factors in youth tends

to track and predict the occurrence of CVD in adulthood.

Vitamin D is crucial to ensure adequate intestinal absorption of calcium and phosphorus and regulate bone mineralization.<sup>10</sup> This is especially important because peak bone mass achieved early in life reduces the risk of osteoporosis in adulthood.<sup>11</sup> Vitamin D has also an important role in decreasing the risk of many chronic illnesses, such as common cancers, autoimmune and infectious diseases, and

CVDs.<sup>12</sup> Epidemiological studies have suggested that low vitamin D status has been associated with metabolic syndrome and its risk factors in children, adults, and morbidly obese men and women.<sup>13–16</sup>

Humans get vitamin D from exposure to sunlight, diet, and dietary supplements.<sup>12</sup> There are two forms of vitamin D—vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol).<sup>17</sup> Vitamin D status depends on the production of vitamin D3 in the skin under the influence of ultraviolet-B radiation from the sun and vitamin D intake through diet or vitamin D supplements. Vitamin D deficiency is common in situations when cutaneous production and intake are compromised; factors related to decreased sun exposure, such as season, latitude, skin type, clothing, and sunscreen barriers, influence cutaneous vitamin D synthesis.<sup>18</sup>

The concentration of 25-hydroxyvitamin D [25(OH)D] in the blood is the best indicator of vitamin D status because it reflects the supply of vitamin D from both the diet and from cutaneous synthesis under the influence of solar ultraviolet-B light.<sup>19,20</sup> Comparing vitamin D intake estimates from foods and dietary supplements to serum 25(OH)D concentrations is difficult because the sun exposure affects vitamin D status; in addition, serum 25(OH)D levels are generally higher than would be predicted on the basis of vitamin D intakes alone.<sup>19</sup> However, the assessment of dietary intake of vitamin D is also important for nutritional epidemiological studies, surveillance, and to design specific nutrient dietary interventions. Indeed, deficiency of vitamin D is now recognized to be highly prevalent worldwide, impacting almost 50% of the general population.<sup>12</sup>

However, little data exist on vitamin D dietary inadequacy, especially for the adolescent population. Therefore, the present study attempts to fill this gap by assessing vitamin D intake and investigating a possible association between vitamin D intake and cardiometabolic risk factors in a sample of Azorean adolescents.

## Methods

### Study design and sampling

Data for the present study derived from a longitudinal school-based study, the Azorean Physical Activity and Health Study II, aimed to evaluate physical activity, physical fitness, and prevalence of overweight/obesity, dietary intake, health-related quality of life, and related factors. Details on the study design and sampling strategy are reported elsewhere.<sup>21</sup> For this study, we only considered the 517 adolescents with metabolic data evaluated in the fall of 2009; of these, 21 did not have valid dietary intake information. Therefore, the final sample included in this cross-sectional analysis comprised 496 adolescents (288 girls and 208 boys) aged 15–18 (mean age, 16.5 ± 0.9).

### Anthropometric measures

Height was measured to the nearest millimeter in bare or stocking feet with the adolescent standing upright against a stadiometer (Holtain Ltd., Crymmych, Pembrokeshire, UK). Weight was measured to the nearest 0.10 kg, with adolescents lightly dressed, using a portable electronic weight scale (Tanita Inner Scan BC 532). Waist circumference measurements were taken as described by Lohman.<sup>22</sup> The waist and height were used to compute the waist-to-height ratio.

### Blood pressure

Blood pressure was measured using a Dynamap vital signs monitors, model BP 8800 (Critikon, Inc., Tampa, Florida). Trained nurses took measurements, and all adolescents were required to sit and rest for at least 5 min prior to blood pressure measurement. Participants were in a seated, relaxed position with their feet resting flat on the ground. Two measurements in the right arm were taken, after 5 and 10 min of rest. The mean of these two measurements was considered. If the two measurements differed by 2 mmHg or more, a third measure was taken.

### Blood sampling

Blood samples were collected from the antecubital vein between 8:00 AM and 10:00 AM, in a sitting position after 10 hr of fasting. Blood samples were processed locally, then stored and shipped to a central laboratory where biochemical evaluation of all study participants was processed. Serum glucose, triglycerides (TGs), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were determined by colorimetric methods using the COBAS INTEGRA 400 Plus (Roche Diagnostics, Indianapolis, IN). The fasting blood insulin levels were measured by a chemiluminescent immunoassay using the IMMULITE 2000 Analyzer (Siemens, Eschborn, Germany). The TC-to-HDL-C ratio was calculated as an index of atherogenic lipid profile.<sup>23,24</sup> The homeostatic model assessment (HOMA), calculated as the product of basal glucose and insulin levels divided by 22.5, was used as a proxy measure of insulin resistance.<sup>25</sup>

### Cardiometabolic risk score

Because there is no consensus regarding the establishment of a universal criterion for the definition of metabolic syndrome in children or adolescents and the prevalence rate is not high, some studies<sup>26,27</sup> have derived a continuous score representing a composite cardiometabolic risk factor profile or index. As some authors have suggested,<sup>26,28,29</sup> the estimation of a cardiometabolic risk score based on the sum of age- and sex-adjusted Z-scores of several metabolic risk factors constitutes a valid tool to identify children and adolescents at risk of developing CVD and T2DM. Indeed, this approach allows the summarization of the cumulative risk that each of the risk factors provides into a continuous score encompassing the overall risk of each individual, and at the same time it accounts, to some extent, for the influence of growth and maturation on the cardiovascular risk factors.<sup>29</sup> In this study, we decided to compute a continuous cardiometabolic risk score from the following measurements: TC-to-HDL-C ratio, TGs, HOMA, systolic blood pressure (SBP), and waist-to-height ratio. For each of these variables, a Z-score was computed by age and sex. Cardiometabolic risk score was constructed by summing the Z-scores of all individual risk factors. High risk was considered when the individual had  $\pm 1$  SD of this score. The score only applies to this study population.

### Dietary intake of vitamin D

Dietary intake was measured with a self-administered semiquantitative food frequency questionnaire (FFQ), validated for the Portuguese adults.<sup>30</sup> This semiquantitative FFQ was designed in accordance with criteria laid out by

Willett et al.<sup>31</sup> and adapted to include a variety of typical Portuguese food items. The FFQ was adapted for adolescents by including foods more frequently eaten by this age group.<sup>32</sup> The adolescent version covered the previous 12 months and comprised 91 food items or beverage categories. For each item, the questionnaire offered nine frequency response options, ranging from “never” to “six or more times per day,” and standard portion size and seasonality. Participants in a free-response section could list any foods not listed in the questionnaire. Energy and nutritional intake were estimated with regard to respondents’ ratings of the frequency, portion, and seasonality of each item using the software Food Processor Plus (ESHA Research Inc., Salem, OR). This program uses nutritional information from the United States that has been adapted for use with typical Portuguese foods and beverages. The vitamin D content of foods was obtained from the Portuguese food composition tables.<sup>33</sup> To verify the interitem consistency, the Cronbach alpha test was applied to the dimensions of the FFQ and the score obtained ( $\alpha=0.892$ ) was high, which indicated a good internal consistency. The estimated average requirement (EAR) of vitamin D was set at 10 mg/day (400 IU) for adolescents.<sup>19</sup> None of the participants reported taking any vitamin D supplements. For the present study, participants were divided into quartiles of vitamin D intake (quartile 1 = £ 3.012 mg/day, quartile 2 = 3.013–4.209 mg/day, quartile 3 = 4.210–6.331 mg/day, and quartile 4 = ‡ 6.332 mg/day).

### Cardiorespiratory fitness

Cardiorespiratory fitness (CRF) was measured using the 20m-Shuttle-Run-Test, as previously described by Léger.<sup>34</sup> This test requires participants to run back and forth between two lines set 20 meters apart. Running speed started at 8.5 km/hr and increased by 0.5 km/hr each minute, reaching 18.0 km/hr at minute 20. Each level was announced on a tape player. The participants were told to keep up with the pace until exhausted. The test was finished when the participant failed to reach the end lines concurrent with the audio signals on two consecutive occasions. Otherwise, the test ended when the subject stopped because of fatigue. Participants were encouraged to keep running as long as possible throughout the course of the test. The number of shuttles (laps) performed by each participant was recorded.

### Pubertal stage

To determine the pubertal stage (ranging from stage 1 to 5), each subject was asked to self-assess his/her stage of secondary sex characteristics. Breast and pubic hair development were assessed according to Tanner’s definitions.<sup>35</sup>

### Statistical analysis

Descriptive data are presented as means and standard deviation unless otherwise stated. All variables were checked for normality and appropriately transformed if necessary. Independent sample t-tests (one-tailed) were performed to compare sex differences in continuous variables, and nominal data were analyzed with chi-squared tests. Binary logistic regression models were constructed to verify the relationship between high cardiometabolic risk score across increasing quartiles of vitamin D intake. Potential confounding variables that were included in the analyses were total energy intake, pubertal stage, fat mass percentage, and CRF. Data

were analyzed using the IBM SPSS Statistic v.20 (SPSS, Chicago, IL). Statistical significance was determined at  $P < 0.05$ .

## Results

Participants’ characteristics are shown in Table 1. Girls had lower mean values of height, weight, waist circumference, TC-to-HDL-C ratio, SBP, glucose, total energy intake, and number of laps, and higher mean values of body fat mass percentage, TC, and HDL-C than boys ( $P < 0.05$  for all). The overall prevalence of participants that achieve the EAR of vitamin D (10 mg/day or 400 IU) was 9.1%, and no sex differences were observed ( $P > 0.05$ ). Odds ratios (OR) for quartiles of vitamin D intake in relation to the high prevalence of cardiometabolic risk score are presented in Table 2. Adolescents in the lowest vitamin D intake quartile group had an OR of 3.35 (95% CI 1.28–8.75) for high cardiometabolic risk score compared with the highest vitamin D intake quartile group after adjustment for total energy intake, pubertal stage, fat mass percentage, and CRF.

## Discussion

To the best of our knowledge, this is the first study assessing associations between vitamin D intake and cardiometabolic risk factors in Portuguese adolescents. The majority of the Azorean adolescents failed to achieve the EAR of vitamin D. The results also showed that the odds ratios for high cardiometabolic risk score increased significantly with the decreasing quartile of vitamin D intake ( $P < 0.05$  for trend), even after adjustment for confounders. Most people meet their vitamin D needs through exposure to sunlight.<sup>36</sup> Season, time of day, length of day, cloud cover, smog, skin melanin content, and sunscreen are among the factors that affect ultraviolet-B radiation exposure and vitamin D synthesis.<sup>19,36</sup> Exposure of arms and legs for 5–30 min (depending on time of day, season, latitude, and skin pigmentation) between the hours of 10 AM and 3 PM twice a week is often adequate.<sup>37,38</sup> Furthermore, above 37° latitude during the months of November through February, there is a marked decrease in ultraviolet-B radiation reaching the earth’s surface. Thus, little vitamin D is produced in the skin during the winter. However, below 37° and closer to the equator, higher vitamin D synthesis occurs in the skin throughout the year.<sup>39</sup>

The Azorean Archipelago is located in the middle of the Northern Hemisphere of the Atlantic Ocean and extends along a west-northwest to east-southeast orientation (between 36.5–43° N and 24.5–31.5° W); therefore, the amount of ultraviolet-B radiation might be insufficient for synthesizing vitamin D. Nevertheless, it has been argued that in fall and winter, diet provided proportionally more vitamin D because of the lack of ultraviolet-B radiation.<sup>40</sup>

In addition, limited exposure to sunlight due to cultural and lifestyle practice may also play a part in etiology of vitamin D deficiency. It is reported that in healthy Caucasian adolescent boys aged 16–18 years, there was a significant association between sports-related sun exposure and vitamin D status.<sup>41</sup> Additionally, a study of Chinese girls aged 15 years also observed that lifestyle factors, such as participation in organized sports and time spent exercising, both at

requirement.

school and in leisure time, showed significant and independent positive association with 25(OH)D concentration.<sup>42</sup>

This can be explained by the fact that most exercise by these subjects was taken outdoors, so that their higher vitamin D status may have resulted from an increased exposure to sunlight. Conversely, there is an awareness of the risks of ultraviolet-B light exposure in childhood and the consequent risk of skin cancer; however, only a small amount of ultraviolet exposure is needed to maintain vitamin D status.<sup>18</sup>

In literature, few studies have investigated the association between vitamin D levels and metabolic syndrome in children and adolescents. All of the studies used the concentration of 25(OH) D in blood as an indicator of vitamin D status. A recent cross-sectional study conducted on 1660, 9-year-old, Korean children reported that low serum vitamin D level appears to be associated with obesity, visceral obesity, hypertriglyceridemia, and metabolic syndrome.<sup>43</sup> Data from the National Health and Nutrition Examination Survey (NHANES) 2001–2004 concluded that low 25(OH)D levels were associated with hyper-tension, hyperglycemia, and metabolic syndrome in the United States adolescent population.<sup>44</sup> Similarly, a study in Caucasian

children also found that central obesity, hypertension, hypertriglyceridemia, low HDL-C levels, and metabolic syndrome were associated with low 25(OH)D levels.<sup>45</sup>

Despite the fact that in our study vitamin D was assessed only by nutritional intake, our results are in line with those of these investigations by showing that adolescents in the lowest vitamin D intake quartile group had an OR of 3.35 for high cardiometabolic risk score compared with the highest vitamin D intake quartile group after adjustment for several confounders. Nevertheless, the association between vitamin D intake and cardiometabolic risk is only significant for the lowest quartile. This result emphasizes the importance of having a tool that can effectively be used to assess the adolescent's vitamin D intake, so that subsequent specific nutrient dietary interventions can take place if the subjects are considered to be vitamin D deficient.

The European Nutrition and Health Report<sup>46</sup> assessed vitamin D intake in children and adolescents from a diversity of studies. Data showed an interval of intakes ranging from 1.2–6.5 mgrams/day in children and adolescents aged 4–14, depending on country, sex, and age group. For instance, in

TABLE 2. ODDS RATIO OF HIGH CARDIOMETABOLIC RISK SCORE ACCORDING TO QUARTILES OF VITAMIN D INTAKE

<i>Variables</i>	<i>OR unadjusted (95% CI)</i>	<i>P for trend</i>	<i>OR adjusted<sup>a</sup> (95% CI)</i>	<i>P for trend</i>
4 <sup>o</sup> Quartile of vitamin D 6.332–36.958 µg/day	1	0.020	1	0.027
3 <sup>o</sup> Quartile of vitamin D 4.210–6.331 µg/day	1.00 (0.45– 2.19)		1.41 (0.57–3.45)	
2 <sup>o</sup> Quartile of vitamin D 3.013–4.209 µg/day	0.68 (0.29–1.61)		1.23 (0.43–3.50)	
1 <sup>o</sup> Quartile of vitamin D 0.927–3.012 µg/day	2.08 (1.03–4.21)		3.35 (1.28–8.75)	

<sup>a</sup>Data were adjusted for total energy intake, pubertal stage, fat mass percentage, and CRF.

To convert vitamin D intakes from µg/day to IU/day, multiply by 40.

OR, odds ratio; CI, confidence interval; 1, reference category; CRF, cardiorespiratory fitness.



Denmark, Germany, Italy, Norway, Poland, Slovenia, Spain, and The Netherlands, mean intakes ranged from 1.5 mg/day in Spanish girls to 7.5 mg/day in Norwegian boys, respectively. In Ireland, the national food surveys in adolescents reported mean vitamin D intakes from food sources of 2.4 and 1.8 mg/day in boys and girls aged 13–17, respectively.<sup>47</sup> In the present study, the interval of vitamin D intakes ranged from 5.5 to 6.2 mg/day in girls and boys, respectively. These results are slightly higher than the studies mentioned above. Nevertheless, these intervals of vitamin D intake are lower than the international recommendations for this age group.

It is generally agreed that the dietary sources of vitamin D in most natural foods are limited, being only present in great amounts in oily fish and the yolks of eggs. To overcome this situation, many countries have their own food fortification policies to improve vitamin D levels. For instance, in the United States, foods such as milk, margarines, orange juice, and yogurt are largely supplemented with vitamin D,<sup>48</sup> which is not the case in Portugal. Considering the high prevalence of inadequate dietary intake of vitamin D in our study, supplementation of vitamin D beyond infancy, especially in adolescents, or fortification of food should be discussed as way to overcome this deficit between actual intakes and the EAR for vitamin D in Azorean adolescents. Accordingly, it is known that well-designed sustainable fortification strategies, which use a range of foods to accommodate diversity, have potential to increase vitamin D intakes across the population distribution and minimize the prevalence of low 25(OH)D levels.<sup>49</sup> This is of importance because it has been shown that optimization of vitamin D status through sun exposure and increased intake of a vitamin D-rich diet can lead to an improved cardiometabolic profile, offering a promising nonpharmacological approach in the prevention of metabolic syndrome,<sup>50</sup> not only in vitamin D-deficient populations but also among populations where vitamin D deficiency has been linked to metabolic risk factors, such as obese children and adolescents.<sup>51</sup>

The strengths of this study include the novelty of assessing the association between vitamin D intake and cardiometabolic risk factors in Azorean adolescents; our analysis was adjusted for important confounders related to cardiometabolic risk such as total energy intake, pubertal stage, fat mass percentage, and CRF. For purposes of epidemiological studies, assessing vitamin D has become important because of the recognition that individuals might not form adequate supplies of vitamin D from exposures to sunlight alone. Furthermore, blood sampling was conducted during the same season (fall). Despite these strengths, this study has some limitations that must be considered when interpreting its results. First, we were unable to assess 25(OH)D level, which is considered to be the best indicator of vitamin D status. Second, the study was cross-sectional and, therefore, causality cannot be inferred. Third, the FFQ relied upon self-reported data from adolescents, and participants may misreport their intake.<sup>52</sup> However, although the FFQ may overestimate total intake, it is a good instrument for ranking intakes<sup>53</sup> as intended in our study. Moreover, Taylor et al.<sup>54</sup> performed a study to determine the validity of a FFQ for assessing calcium and vitamin D intake in 12- to 18-year-old anorexic and healthy girls. Their results demonstrated that the FFQ was useful in maximizing the information regarding calcium and vitamin D intake in a segment of the population that is vulnerable to nutrient deficiencies. Last, sun exposure is another important source

of vitamin D; however, wearing a sunscreen with a sun protection factor was not assessed in our study.

## Conclusions

The results of this study indicate that the majority of the Azorean adolescents failed to achieve the recommended nutrient intake of vitamin D, and adolescents in the lowest vitamin D intake quartile had a higher cardiometabolic risk score compared with the highest vitamin D intake quartile, after adjustment for several confounders.

Considering the low proportion of adolescents who met nutrient intake of vitamin D in this study, more work is needed to ensure that adolescents are consuming sufficient vitamin D, because lower levels of vitamin D intake were associated with worse metabolic profile among Azorean adolescents. Portuguese policy makers should discuss food fortification and supplementation as a possibility to overcome this public health problem.

## Acknowledgments

This study was supported by grants from the FCT-MCTES: BD/44422/2008; BPD/65180/2009; BSAB/1025/2010, PEStOE/SAU/UI0617/2011, and the Azorean Government.

## Author Disclosure Statement

No competing financial interests exist.

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