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Prediction of winter vitamin D status and requirements in the UK population based on 25(OH) vitamin D half-life and dietary intake data

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ABSTRACT

On a population basis, there is a gradual decline in vitamin D status (plasma 25(OH)D) throughout winter. We developed a mathematical model to predict the population winter plasma 25(OH)D concentration longitudinally, using age-specific values for 25(OH)D expenditure (25(OH)D_3 $t_{1/2}$), cross-sectional plasma 25(OH)D concentration and vitamin D intake (VDI) data from older (70+ years; n = 492) and younger adults (18–69 years; n = 448) participating in the UK National Diet and Nutrition Survey. From this model, the population VDI required to maintain the mean plasma 25(OH)D at a set concentration can be derived. As expected, both predicted and measured population 25(OH)D (mean (95%CI)) progressively declined from September to March (from 51 (40–61) to 38 (36–41) nmol/L (predicted) vs 38 (27–48) nmol/L (measured) in older people and from 59 (54–65) to 34 (31–37) nmol/L (predicted) vs 37 (31–44) nmol/L (measured) in younger people). The predicted and measured mean values closely matched. The predicted VDIs required to maintain mean winter plasma 25(OH)D at 50 nmol/L at the population level were 10 (0–20) to 11 (9–14) and 11 (6–16) to 13(11–16) μg/d for older and younger adults, respectively dependent on the month. In conclusion, a prediction model accounting for 25(OH)D_3 $t_{1/2}$, VDI and scaling factor for the 25(OH)D response to VDI, closely predicts measured population winter values. Refinements of this model may include specific scaling factors accounting for the 25(OH)D response at different VDIs and as influenced by body composition and specific values for 25(OH)D_3 $t_{1/2}$ dependent on host factors such as kidney function. This model may help to reduce the need for longitudinal measurements.

1. Introduction

The plasma concentration of 25 hydroxy vitamin D (25(OH)D) reflects the supply from oral intake (in the form of vitamin D_2 and D_3 and 25(OH)D_3)) and vitamin D3 from endogenous cutaneous synthesis. In temperate climates (>30°N and >30°S), no cutaneous synthesis of vitamin D takes place in the winter months [1]. Therefore, the winter plasma concentration of 25(OH)D is mainly a function of an individual's post-summer status, their expenditure of 25(OH)D and their vitamin D supply through diet. In populations living in a temperate climate, there is a gradual decline in the mean vitamin D status from late autumn throughout winter [1–4], indicating that, on average, the daily vitamin D intake is less than its daily expenditure. The impact of this circannual cycling of 25(OH)D is uncertain [5], but many advocate that a decrease in plasma 25(OH)D below the threshold of sufficiency (50 nmol/L) or deficiency (30 nmol/L), as defined by The Institute of Medicine (IOM) [6], should be avoided throughout the year to prevent a winter increase in plasma parathyroid hormone and bone resorption, although the threshold at which this occurs is disputed [5–9].

Here we present a mathematical model to predict longitudinally the population plasma 25(OH)D concentration during winter. Plasma 25(OH)D concentrations and vitamin D intake (VDI) data from older (70+ years) and younger adults (18–69 years) participating in the population based UK National Diet and Nutrition Survey (NDNS) [10,11] and age-specific values for vitamin D expenditure measured as 25(OH)D half-life (25(OH)D_3 $t_{1/2}$) [12,13]. This model was further applied to estimate mathematically the required vitamin D intake to maintain the population mean plasma 25(OH)D at a set concentration.

2. Methods

A subset of data from the National Diet and Nutrition Survey (NDNS) rolling programme (NDNS years 1–3; 2008/9–2010/11) and the NDNS of people age 65 years and over (1994/1995) was extracted from the full data sets available from the UK Data Service.

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The dataset included 25(OH)D concentration, month of blood collection, age and dietary intakes of vitamin D (VDI) for each participant. Special permission to include the month of blood collection was granted (personal communication Public Health England NDNS project board). Only data of individuals of 18 years of age and over were selected. Further information about the survey, how to access the data and to obtain permission for their use, can be found at https://www.noo.org.uk/data_sources/Nutrition/NDNS and http://www.data-archive.ac.uk. Recruitment of participants to NDNS, methods of data collection, measurement of 25(OH)D concentration and dietary intake of vitamin D are described elsewhere [10,11] and available online (http://webarchive.nationalarchives.gov.uk/20130402145952/ http://transparency.dh.gov.uk/category/statistics/ndns/) and http://www.data-archive.ac.uk.

In brief, NDNS participants were randomly selected from the UK population; data were collected from each individual once, i.e. on a cross-sectional basis. The survey was designed to be nationally representative. Visits took place throughout the year and the dates of visits and blood collections were recorded. Written and verbal consent was obtained from all participants. To ensure anonymity, the NDNS dataset only contains details about the month of blood collection not the day; therefore they were all assigned a value 1, i.e. all September dates were entered in the model as September 1. A venous blood sample was collected non-fasting and the plasma 25(OH)D concentration was measured using Diasorin (DiaSorin Ltd, Dartford, UK) Liaison chemiluminesence immune assay (NDNS year 1–3; 2008/9–2010/11) or Diasorin Radio – immune assay (NDNS: people age 65 years and over (1994/1995)) in lithium heparin plasma. Cross-calibration of the two Diasorin assays showed good agreement and no systematic bias (https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-results-from-years-1-to-4-combined-of-the-rolling-programme-for-2008-and-2009-to-2011-and-2012). The laboratory performing these assays was DEQAS accredited.

Participants completed a 4-day weighed food diary of all food and drink consumed using standardised house hold scales as described in detail in the above referenced NDNS report and this is considered to represent habitual nutrient intakes on a population level [14]. Vitamin D intake was assessed as Vitamin D (<2002) or the Vitamin D equivalents to include 25(OH)D3 from animal tissues (>2002) using British food composition tables (http://www.ifr.ac.uk/fooddatabanks/nutrients.htm#.Unn_QobTQil).

The data set was split by age into a subset of older (70+ years) and younger adults (18–69 years). For initial inspection of the data to determine the yearly peak and nadir in the plasma concentration of 25(OH)D and potential seasonal variation in vitamin D intake, data for all months were used. For data modelling, only data of individuals who provided a blood sample between September and March and had completed a food diary were used (70+ years; n = 492) and younger adults (18–69 years; n = 448).

2.1. Mathematical model to predict the population plasma 25(OH)D concentration in winter

The following mathematical model was developed as modification of the algorithm proposed by Diffey [15,16]. Only autumn and winter values (October to March) were modelled, with plasma concentrations obtained in September to April as starting value as explained below. The contribution of cutaneous vitamin D synthesis was assigned a value of zero. The resulting model gives the prediction plasma concentration of 25(OH)D at any time point (t) after a measured value was obtained (which was defined as t = 0) and contains 2 main components. The first component accounts for the decline in plasma 25(OH)D due to its expenditure, assuming first order kinetics. Age-specific mean values for 25(OH)D_3 $t_{1/2}$ were used, as experimentally obtained with a stable isotope technique with LC–MS/MS quantification[12,13]. The second term accounts for the daily increment in plasma 25(OH)D derived from an individual's dietary intake of vitamin D and the subsequent exponential decline of this component, as reflected by the sum of the geometric series. It accounts for the plasma 25(OH)D response to vitamin D intake (R (oral)), using a fixed dose-response rate (the scaling factor) and the release of 25(OH)D into plasma of the fraction stored in tissues.

$$\text{Plasma } 25(\text{OH})\text{D}_{(t)} = [\text{Plasma } 25(\text{OH})\text{D}_{(t=0)} \times e^{-kt}] + (0.168 \times \text{VDI}) \times \left(\frac{(1-e^{-kt})}{(1-e^{-k})}\right)$$

In which:

$$\boldsymbol{k} = \frac{ln2}{25(\text{OH})\text{D3t1/2}}$$

in which 25(OH)D_3 $t_{1/2}$ is the age specific 25(OH)D_3 half-life.

t = the number of days since t = 0

VDI is the daily vitamin D intake calculated as the mean of the 4 recorded days

(0.168* VDI)*((1-e^{-kt})/(1-e^{-k})) reflects the daily increment in plasma 25(OH)D due to VDI and the subsequent exponential decline of this component. The latter was described by the sum of the geometric series ((1-e^{-kt})/(1-e^{-k})) in which k was used as defined above.

The conversion factor of 0.168 (R(oral)) was derived from:

$$R(\text{oral}) = S \times (1\text{-}f) \times 2^{-t/\beta} + (f \times 2^{-t/Y}) = 0.168$$

In which:

S was set as = 0.023; S is the scaling factor for the 25(OH)D plasma response to VDI and was derived from the median conversion factor from 9 dose-response studies [15].

f is the fraction of vitamin D taken up and stored in tissues = 0.15

β is 25(OH)D_3 $t_{1/2}$ as defined above

Y is tissue half-life of vitamin D = 250 days

The plasma 25(OH)D concentration was expressed in nmol/L; 25(OH)D_3 $t_{1/2}$ in days; VDI in μg/d.

The plasma 25(OH)D concentration for each participant as measured in NDNS was included in the model as the starting value (t = 0) and the predicted values were progressively calculated for each day thereafter, i.e. if a blood sample was collected in September, predicted data were derived from this month onwards; if collected in November, predicted values were derived for the months thereafter only. As a consequence, the number of individuals included in the model progressively increased at each month.

The following assumptions were made:

(ii) A linear relationship between the increment in plasma 25 (OH)D and VDI was assumed within the range of vitamin D intakes observed in this survey. Therefore a fixed value for S was used. This was based on the *meta*-regression analyses presented in the IOM report, describing a biphasic response with a different dose-response below and over 25 μg/d (1000 IU/d) [6]. This can be explained by the metabolic conversion of vitamin D to 25(OH)D, changing from first to zero order kinetics due to saturation of the hepatic 25-hydoxylase [17]. We also did not account for the potential difference in the response to food based or supplemental supply of vitamin D [18]. (ii) A constant supply of vitamin D into the blood stream from the diet and subsequent conversion in 25(OH)D was assumed; therefore no allowance was made for the delay between ingestion and plasma appearance of plasma 25(OH)D and/or peaks in vitamin D intake during specific time slots and days. (iii) The plasma 25(OH)D decreases exponentially starting at