

## Vitamin D deficiency in Europe: pandemic?<sup>1,2</sup>

Kevin D Cashman,<sup>3,4\*</sup> Kirsten G Dowling,<sup>3</sup> Zuzana Škrabáková,<sup>3</sup> Marcela Gonzalez-Gross,<sup>6,7</sup> Jara Valtueña,<sup>6</sup> Stefaan De Henauw,<sup>8</sup> Luis Moreno,<sup>9</sup> Camilla T Damsgaard,<sup>10</sup> Kim F Michaelsen,<sup>10</sup> Christian Mølgaard,<sup>10</sup> Rolf Jorde,<sup>11</sup> Guri Grimnes,<sup>11</sup> George Moschonis,<sup>12</sup> Christina Mavrogianni,<sup>12</sup> Yannis Manios,<sup>12</sup> Michael Thamm,<sup>13</sup> Gert BM Mensink,<sup>13</sup> Martina Rabenberg,<sup>13</sup> Markus A Busch,<sup>13</sup> Lorna Cox,<sup>14</sup> Sarah Meadows,<sup>14</sup> Gail Goldberg,<sup>14</sup> Ann Prentice,<sup>14</sup> Jacqueline M Dekker,<sup>15</sup> Giel Nijpels,<sup>16</sup> Stefan Pilz,<sup>18</sup> Karin M Swart,<sup>15</sup> Natasja M van Schoor,<sup>15</sup> Paul Lips,<sup>17</sup> Gudny Eiriksdottir,<sup>19</sup> Vilundur Gudnason,<sup>19,20</sup> Mary Frances Cotch,<sup>21</sup> Seppo Koskinen,<sup>23</sup> Christel Lamberg-Allardt,<sup>24</sup> Ramon A Durazo-Arvizu,<sup>25</sup> Christopher T Sempos,<sup>22</sup> and Mairead Kiely<sup>3,5</sup>

<sup>3</sup>Cork Centre for Vitamin D and Nutrition Research, School of Food and Nutritional Sciences, <sup>4</sup>Department of Medicine, and <sup>5</sup>Irish Centre for Fetal and Neonatal Translational Research, University College Cork, Cork, Ireland; <sup>6</sup>ImFINE Research Group, Department of Health and Human Performance, Technical University of Madrid, Madrid, Spain; <sup>7</sup>CIBER: CB12/03/30038 Fisiopatología de la Obesidad y la Nutrición, CIBERobn, Instituto de Salud Carlos III, Madrid, Spain; <sup>8</sup>Department of Public Health, Ghent University, Ghent, Belgium; <sup>9</sup>Growth, Exercise, Nutrition and Development Research Group, Faculty of Health Sciences, University of Zaragoza, Zaragoza, Spain; <sup>10</sup>Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Frederiksberg C, Denmark; <sup>11</sup>Tromsø Endocrine Research Group, Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø, Norway; <sup>12</sup>Department of Nutrition and Dietetics, Harokopio University, Athens, Greece; <sup>13</sup>Department of Epidemiology and Health Monitoring, Robert Koch-Institut, Berlin, Germany; <sup>14</sup>Medical Research Council Human Nutrition Research Unit, Elsie Widdowson Laboratory, Cambridge, United Kingdom; <sup>15</sup>Department of Epidemiology and Biostatistics, EMGO Institute for Health and Care Research, <sup>16</sup>Department of General Practice & Elderly Care Medicine, and <sup>17</sup>Department of Internal Medicine, Section of Endocrinology, Vrije Universiteit University Medical Center, Amsterdam, Netherlands; <sup>18</sup>Division of Endocrinology and Metabolism, Department of Internal Medicine, Medical University of Graz, Graz, Austria; <sup>19</sup>Icelandic Heart Association, Kopavogur, Iceland; <sup>20</sup>University of Iceland, Reykjavik, Iceland; <sup>21</sup>Division of Epidemiology and Clinical Applications, National Eye Institute and <sup>22</sup>Office of Dietary Supplements, NIH, Bethesda, MD; <sup>23</sup>Department of Health, Functional Capacity and Welfare and Department of Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki, Finland; <sup>24</sup>Department of Food and Environmental Sciences, Helsinki University, Helsinki, Finland; and <sup>25</sup>Department of Public Health Sciences, Loyola University Stritch School of Medicine, Chicago, IL

### ABSTRACT

**Background:** Vitamin D deficiency has been described as being pandemic, but serum 25-hydroxyvitamin D [25(OH)D] distribution data for the European Union are of very variable quality. The NIH-led international Vitamin D Standardization Program (VDSP) has developed protocols for standardizing existing 25(OH)D values from national health/nutrition surveys.

**Objective:** This study applied VDSP protocols to serum 25(OH)D data from representative childhood/teenage and adult/older adult European populations, representing a sizable geographical footprint, to better quantify the prevalence of vitamin D deficiency in Europe.

**Design:** The VDSP protocols were applied in 14 population studies [reanalysis of subsets of serum 25(OH)D in 11 studies and complete analysis of all samples from 3 studies that had not previously measured it] by using certified liquid chromatography–tandem mass spectrometry on biobanked sera. These data were combined with standardized serum 25(OH)D data from 4 previously standardized studies (for a total  $n = 55,844$ ). Prevalence estimates of vitamin D deficiency [using various serum 25(OH)D thresholds] were generated on the basis of standardized 25(OH)D data.

**Results:** An overall pooled estimate, irrespective of age group, ethnic mix, and latitude of study populations, showed that 13.0% of the 55,844 European individuals had serum 25(OH)D concentrations  $<30$  nmol/L on average in the year, with 17.7% and 8.3% in those sampled during the extended winter (October–March) and summer (April–November) periods, respectively. According to an alternate suggested definition of vitamin D deficiency ( $<50$  nmol/L), the prevalence was 40.4%. Dark-skinned ethnic subgroups had

much higher (3- to 71-fold) prevalence of serum 25(OH)D  $<30$  nmol/L than did white populations.

**Conclusions:** Vitamin D deficiency is evident throughout the European population at prevalence rates that are concerning and that require action from a public health perspective. What direction these strategies take will depend on European policy but should aim to ensure vitamin D intakes that are protective against vitamin D deficiency in the majority of the European population. *Am J Clin Nutr* 2016;103:1033–44.

**Keywords:** vitamin D deficiency, prevalence, 25(OH)D, standardized, Europe

<sup>1</sup> Supported by funding from the European Commission under its Seventh Framework Programme (Food-based solutions for optimal vitamin D nutrition and health through the life cycle; grant 613977). The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the NIH, the US Department of Health and Human Services, or the US Department of Commerce. This is a free access article, distributed under terms (<http://www.nutrition.org/publications/guidelines-and-policies/license/>) that permit unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

<sup>2</sup> Supplemental Material and Supplemental Figures 1–2 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://ajcn.nutrition.org>.

\*To whom correspondence should be addressed. E-mail: [k.cashman@ucc.ie](mailto:k.cashman@ucc.ie)

Received August 4, 2015. Accepted for publication December 28, 2015.

First published online February 10, 2016; doi: 10.3945/ajcn.115.120873.

## INTRODUCTION

Vitamin D is the nutrient that has captured the attention of the scientific and medical communities, regulatory agencies, the food industry, and the public alike over the past 15 y. This is evidenced by the explosion of scientific literature, a dramatic increase in physician-requested tests for patient vitamin D status in some countries, a number of authoritative re-evaluations of dietary recommendations, and sales of vitamin D supplements and the increased number of vitamin D–fortified food products coming on the market. Vitamin D deficiency has been described as being pandemic (1), with associated direct and indirect costs for Europe estimated to be running at hundreds of billion Euro (2).

Vitamin D deficiency has been variably defined as possessing a serum 25-hydroxyvitamin D [25(OH)D,<sup>26</sup> the biochemical index of vitamin D status (3)] concentration <25 to <75 nmol/L (4). Knowledge of the distributions of serum 25(OH)D concentrations in representative populations, with appropriate consideration of sex, life stage, ethnicity, and seasonality, is critical for the quantification of vitamin D deficiency as well as for devising effective strategies for its prevention (4, 5). However, serum 25(OH)D distribution data for the European Union are of variable quality, making it difficult to estimate the prevalence of vitamin D deficiency across member states. For example, a recent systematic review of vitamin D status in populations worldwide clearly showed that the variability in mean serum 25(OH)D concentrations across European countries was large, and even within a country, the variability from different studies ranged from 10% to 300% (6). Although there are many likely contributory reasons for differences in vitamin D deficiency prevalence estimates between populations, differences in analytic method for serum 25(OH)D are likely to contribute (4). In addition, several reports have shown that available 25(OH)D assays can yield markedly differing results (7–10).

Calls have been made to use centralized laboratories to make an international comparison of serum 25(OH)D and vitamin D deficiency prevalence estimates more reliable (11), but this approach might not be feasible, given existing national structures and systems. As a consequence of these widespread, method-related differences in results of serum 25(OH)D (7–10), the NIH-led international Vitamin D Standardization Program (VDSP) developed protocols for standardizing 25(OH)D measurement in national health/nutrition surveys around the world, as have been described in detail elsewhere (4, 12). Their recent application to serum 25(OH)D data from the Irish National Adult Nutrition Survey showed that the yearly prevalence of serum 25(OH)D <30 nmol/L [the US Institute of Medicine's definition of vitamin D deficiency (13)] increased from 6.5% (via the original immunoassay measurement) to a projected 11.4% (14). Importantly, reanalysis of all serums in the survey ( $n = 1118$ ) by our certified liquid chromatography–tandem mass spectrometry (LC-MS/MS) method confirmed the true prevalence estimate as 11.2%, which was almost twice as high as the immunoassay-based estimate and almost identical to the VDSP projection (14).

Thus, the VDSP approach, if coupled with key representative population studies, provides the potential for generation of prevalence estimates of vitamin D deficiency in Europe by using standardized serum 25(OH)D data. This would permit quantification of the magnitude of the public health problem and a solid platform on which to build public health policy aimed at preventing vitamin D deficiency in Europe. Accordingly, our objective was to apply the VDSP protocols to existing serum 25(OH)D data from 18 key (identified nationally or regionally) representative studies of European children, teenagers, adults, and older adults ( $n = 55,844$  individuals).

## METHODS

### Studies included and categorizations applied

Within the VDSP, nationally representative nutrition and health surveys are prioritized; however, some member states in Europe do not have such surveys with nationally representative data on serum 25(OH)D concentrations. Thus, in the absence of such data, well-curated samples from regionally representative health surveys can also achieve some degree of population coverage. Our present work is part of the European Commission–funded integrated project, Food-based solutions for optimal vitamin D nutrition and health through the life cycle (ODIN; [www.odin-vitd.eu](http://www.odin-vitd.eu)). One of the primary aims of ODIN was to quantify the prevalence of vitamin D deficiency in European populations by using standardized serum 25(OH)D values as a key prioritized existing knowledge gap. The project included a number of identifiable nationally representative nutrition and health surveys in addition to regionally representative health surveys from various European member states and of different life stage groups, which were of strategic importance for European coverage (a brief description of each of the studies, including their full names, acronyms, and country of origin, is provided in the **Supplemental Material**). The 14 European childhood and teenage as well as adult and older adult study populations, identified as a priority to obtain data on standardized serum 25(OH)D data, are as follows:

1. Healthy Lifestyle in Europe by Nutrition in Adolescence study (9 European countries) (15, 16)
2. Optimal well-being, development and health for Danish children through a healthy New Nordic Diet School Meal Study (Denmark) (17, 18)
3. Tromsø Study: Fit Futures (Norway) (19–21)
4. Healthy Growth Study (Greece) (22)
5. Infant's Nourishment and Nutritional Status study (Greece) (23)
6. Cork BASELINE Birth Cohort Study (Ireland) (24)
7. German Health Interview and Examination Survey for Children and Adolescents (Germany) (25)
8. National Diet and Nutrition Survey (NDNS): Years 1–4 (combined) of the Rolling Program (2008/2009–2011/12) (United Kingdom) (26)
9. German Health Interview and Examination Survey for Adults (Germany) (27, 28)

<sup>26</sup> Abbreviations used: LC-MS/MS, liquid chromatography–tandem mass spectrometry; NDNS, National Diet and Nutrition Survey; ODIN, Food-based solutions for optimal vitamin D nutrition and health through the life cycle; VDSP, Vitamin D Standardization Program; 25(OH)D, 25-hydroxyvitamin D.

10. Tromsø Study–6th Survey (Tromsø 6) (Norway) (19, 29–31)
11. New Hoorn Study (Netherlands) (32)
12. Longitudinal Aging Study Amsterdam (Netherlands) (33)
13. Age, Gene/Environment Susceptibility–Reykjavik study (Iceland) (34)
14. Finnish Migrant Health and Wellbeing Study (Maamu) (Finland) (35, 36)

The key summary demographic characteristics (age, sex distribution, ethnicity, and season of blood sampling) of these 14 studies are shown in **Table 1**. We also had vitamin D deficiency prevalence data from 4 additional European studies, on which we had previously standardized serum 25(OH)D data by using the same VDSP approach (14, 37), and we combined these data with data from the 14 new studies in generating a pooled estimate in the present work. The descriptions of these other 4 studies [National Adult Nutrition Survey, Ireland; Health 2011, Finland; HUBRO (Oslo Health Study), Oslo, Norway; and Health2006, Copenhagen, Denmark] have been reported in detail elsewhere (14, 37). None of the 18 studies included pregnant women or older adults in care homes.

Winter and spring represent the seasons during which vitamin D status declines and reaches its nadir, typically in late winter/early spring (38). Thus, the present work applied a wider definition capturing an extended winter (i.e., November–March) and an extended summer period (i.e., April–October), where appropriate. In the present work, we classified population samples as being of young children if the participants were aged 1–6 y, older children as 7–14 y, and teenagers as 15–18 y, in line with that applied by the European Food Safety Agency in their Dietary Reference Values (39). Adult populations were those with participants aged  $\geq 19$  y.

Categories of ethnicity varied across the population samples, and thus in the present work, a “white” and “nonwhite” categorization was applied. The nonwhite category included those recorded as being black, Asian, or other, including mixed race. The exception to this categorization was within the ethnic Maamu sample, where the study, by design, included 3 Finnish ethnic immigrant groups: white Russian speaking, Kurdish, and Somali (36). Details of the method used for the original serum/plasma total 25(OH)D analysis are also shown in Table 1.

#### Applying the VDSP protocol for standardization of serum 25(OH)D data from past surveys to the study populations

The VDSP protocol for standardization of serum 25(OH)D data from past surveys, as used by some of us previously on the Irish national serum 25(OH)D data ( $n = 1118$ ) (14) and that of Finnish white adults ( $n = 4102$ ) (37), as well as regionally representative adult samples in Copenhagen, Denmark ( $n = 3409$ ), and Oslo, Norway ( $n = 1042$ ) (37), and again in this study, are outlined in detail elsewhere (4, 12) but can be briefly summarized as follows: the protocols conduct a within-quartile uniform sampling procedure of the serum 25(OH)D data from the entire survey sample (40) to select a subset of 100–175 biobanked serum samples for reanalysis of 25(OH)D by a standardized and certified LC-MS/MS method, which is traceable to the National Institute of Standards and Technology higher-order Reference Measurement Procedure (4, 12). The results are used

to develop master regression equations, which then recalibrate the existing 25(OH)D data set for the entire survey sample.

The LC-MS/MS method at University College Cork used in this study for all samples, except those from the United Kingdom’s NDNS, is certified by the CDC’s Vitamin D Standardization Certification Program (41). Because the LC-MS/MS method at the NDNS laboratory at the Medical Research Council Human Nutrition Research Unit, Cambridge, was also standardized against the National Institute of Standards and Technology higher-order Reference Measurement Procedure through the VDSP, this was used for their sample reanalysis to use the biobanked samples as efficiently as possible [ $R^2 = 0.997$ ; University College Cork measured (25[OH]D) =  $0.968 \times$  Human Nutrition Research Unit measured (25[OH]D) + 0.806;  $n = 50$  (VDSP Seattle sera [4])].

In addition to the 11 studies for which the existing serum 25(OH)D data were standardized, the biobanked sera from 3 study populations (Infant’s Nourishment and Nutritional Status, BASELINE, and New Hoorn Study) were analyzed de novo by the certified LC-MS/MS method and thus did not require a calibration equation. The standardized data from 14 studies included in the present work ( $n = 46,173$ ) plus the 4 studies previously standardized by us with the VDSP approach ( $n = 9671$ ) (14, 37) were used in estimating prevalence. In both human serum and plasma, 25(OH)D metabolites have been shown to be stable when stored frozen (42) and when subjected to multiple freeze-thaw cycles (43). In addition, Hollis (44) has reported that long-term ( $>10$ -y) storage of pooled human 25(OH)D internal controls at  $-20^\circ\text{C}$  led to no detectable degradation of 25(OH)D.

#### Serum 25(OH)D thresholds

Original and standardized serum 25(OH)D concentrations were compared with cutoffs for 25(OH)D as per the US Institute of Medicine Dietary Reference Intake committee’s definitions: persons are at risk of deficiency at serum 25(OH)D concentrations  $<30$  nmol/L, whereas 40 and 50 nmol/L are consistent with that needed by 50% and 97.5% of individuals aged  $>1$  y, respectively, in terms of bone health (13). In addition, a serum 25(OH)D concentration  $<25$  nmol/L has also been a traditional cutoff used in Europe to define vitamin D deficiency on the basis of metabolic bone disease (45, 46) and thus was also included. Because the Task Force for the Clinical Guidelines Subcommittee of The Endocrine Society has suggested that to maximize the effect of vitamin D on calcium, bone, and muscle metabolism, serum 25(OH)D concentration should exceed 75 nmol/L (47), we also used this cutoff for comparison purposes. The same task force suggests  $<50$  nmol/L as vitamin D deficiency (47).

#### Data and statistical analysis

Data and statistical analysis was conducted by using STATA 12 (StataCorp LP) and CBStat5 (Kristian Linnet). A statistical algorithm, developed within the VDSP and published recently (40), for estimating the number of stored samples that need to be reanalyzed was used. The maximum projected sample size of stored serum samples required for the VDSP protocol and with this collection of population studies was calculated by using procedures for the estimation of the predicted LC-MS/MS–based

**TABLE 1**  
 Characteristics of the studies for standardization of serum 25(OH)D concentrations in European populations<sup>1</sup>

Study [year(s) of study] (ref)	Region/country (latitude)	N	Age, y	Sex, female: male, %	Ethnicity, white: nonwhite, %	Season of sampling, %	Original 25(OH)D method
HELENA [2006–2007] (15, 16)	10 EU Centres <sup>2</sup> (35–59°N)	1006	14.7 ± 1.2 (12.5–17.4) <sup>3</sup>	53.2:46.8	93.3:4.8 <sup>4</sup>	Winter: 21.9 Spring: 45.6 Summer: 9.0 Autumn: 23.5	IDS ELISA
OPUS School Meal Study [2011–2012] (17, 18)	Eastern Denmark (54–55°N) (regionally representative)	779 <sup>5</sup>	10.0 ± 0.6 (8.4–11.6) <sup>5</sup>	47.8:52.2 <sup>5</sup>	94.7:5.3 <sup>5</sup>	Baseline visit <sup>5</sup> Winter: 0.0 Spring: 2.7 Summer: 97.3 Autumn: 0.0	DiaSorin Liaison
Tromsø Study: Fit Futures [2010–2011] (19–21)	Tromsø/Norway (69°N) (regionally representative)	890	16.0 ± 1.0 (15.0–18.0)	46.6:53.4	97.1:1.9 <sup>4</sup>	Winter: 45.7 Spring: 24.2 Summer: 0.0 Autumn: 30.1	LC-MS/MS
HGS [2007–2009] (22)	Athens, Crete, Thessaloniki/Greece (35–40°N) (regionally representative)	806	11.2 ± 0.6 (9.4–13.7)	52.2:47.8	98.5:1.5	Winter: 21.3 Spring: 51.1 Summer: 1.9 Autumn: 25.7	Roche Elecsys
INNS [2005–2007] (23)	Athens/Greece (37°N) (regionally representative)	222	4.5 ± 0.6 (3.0–5.9)	46.0:54.0	99.1:0.9	Winter: 37.4 Spring: 36.5 Summer: 0.4 Autumn: 25.7	NA (measured de novo)
Cork BASELINE Birth Cohort Study [2008–2011] (24)	Cork/Ireland (51°N)	742	2.1 ± 0.1 (1.9–2.8)	47.2: 52.8	98.9: 1.1	Winter: 22.2 Spring: 24.7 Summer: 22.2 Autumn: 30.9	NA (measured de novo)
KiGGS [2003–2006] (25)	Germany (47–55°N) (nationally representative)	10,015	9.5 ± 4.6 (1–17)	49.0:51.0	NA	Winter: 24.4 Spring: 21.9 Summer: 24.3 Autumn: 29.4	DiaSorin Liaison
NDNS: Rolling Program Years 1–4 [2008–2012] (26)	United Kingdom (50–59°N) (nationally representative)	511 <sup>6</sup>	11.6 ± 4.7 (1–18) <sup>6</sup>	45.4:54.6 <sup>6</sup>	87.7:12.3 <sup>6</sup>	Winter: 25.4 <sup>6</sup> Spring: 25.6 Summer: 23.7 Autumn: 25.2 <sup>4</sup>	DiaSorin Liaison
NDNS: Rolling Program Years 1–4 [2008–2012] (26)	United Kingdom (50–59°N) (nationally representative)	977 <sup>6</sup>	50.5 ± 16.0 (19–91) <sup>6</sup>	53.4:46.6 <sup>6</sup>	93.2:6.8 <sup>6</sup>	Winter: 24.1 <sup>6</sup> Spring: 26.0 Summer: 25.3 Autumn: 24.7 <sup>4</sup>	DiaSorin Liaison
DEGS [2008–2011] (27, 28)	Germany (47–55°N) (nationally representative)	6995	50.6 ± 16.6 (18–79)	52.0:48.0	NA	Winter: 22.7 Spring: 24.8 Summer: 20.9 Autumn: 31.6	DiaSorin Liaison

(Continued)

TABLE 1 (Continued)

Study [year(s) of study] (ref)	Region/country (latitude)	N	Age, y	Sex,		Ethnicity,		Season of sampling, %	Original 25(OH)D method
				female: male, %	white: nonwhite, %				
Tromsø Study—6th Survey [2008] (29–31)	Norway (69°N) (regionally representative)	12,817	57.5 ± 12.6 (30–87)	46.7:53.3	100.0:0.0	Winter: 24.6 Spring: 21.4 Summer: 16.3 Autumn: 37.7	Roche ECLIA		
NHS [2006–2007] (32)	Netherlands (52°N) (regionally representative)	2625	53.4 ± 6.7 (40–66)	53.6:46.4	95.8:4.2	Winter: 26.2 Spring: 14.2 Summer: 26.3 Autumn: 33.3	NA (measured de novo)		
LASA [2009] (33)	Netherlands (52°N) (nationally representative)	915	71.4 ± 7.7 (61–99)	53.4:46.6	96.8:3.0 <sup>4</sup>	Winter: 7.5 Spring: 28.8 Summer: 40.2 Autumn: 22.8 <sup>4</sup>	DiaSorin Liaison		
AGES-Reykjavik [2002–2006] (34)	Iceland (64°N) (regionally representative)	5519	76.6 ± 5.6 (66–96)	57.3:42.7	100.0:0.0	Winter: 25.5 Spring: 26.5 Summer: 15.1 Autumn: 32.9	DiaSorin Liaison		
Finnish Migrant Health and Wellbeing Study (Maamu) [2010–2012] (35, 36)	Finland (60–63°N) (representative of the immigrant populations in 6 Finnish cities)	1310	37.0 ± 12.0 (18–64)	56.5:43.5	Ethnic <sup>7</sup>	Winter: 32.2 Spring: 32.5 Summer: 12.4 Autumn: 23.9	Architect chemiluminescent		

<sup>1</sup>AGES, Age, Gene/Environment Susceptibility; DEGS, German Health Interview and Examination Survey for Adults; EU, European Union; HELENA, Healthy Lifestyle in Europe by Nutrition in Adolescence; HGS, Healthy Growth Study; INNS, Infant's Nourishment and Nutritional Status; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; LASA, Longitudinal Aging Study Amsterdam; LC-MS/MS, liquid chromatography–tandem mass spectrometry; NA, not applicable; NDNS, National Diet and Nutrition Survey; NHS, New Hoorn Study; OPUŠ, Optimal well-being, development and health for Danish children through a healthy New Nordic Diet; ref, reference; 25(OH)D, 25-hydroxyvitamin D.

<sup>2</sup>Athens (Greece), Dortmund (Germany), Ghent (Belgium), Heraklion (Greece), Lille (France), Pecs (Hungary), Rome (Italy), Stockholm (Sweden), Vienna (Austria), and Zaragoza (Spain).

<sup>3</sup>Mean ± SD; range in parentheses (all such values).

<sup>4</sup>Overall percentage <100% as data not reported for some subjects.

<sup>5</sup>OPUS sample at 3-mo visit: *n* = 386; female:male: 46.9%:53.1%; white:nonwhite: 93.3%:6.7%; sampled in winter, spring, summer, autumn: 80.9%, 12.4%, 0%, and 6.7%, respectively.

<sup>6</sup>The NDNS was of individuals aged ≥1.5 y, but for this work, to allow comparison with other children and adult/older adult populations, the sample was stratified into 1–18 and >19 y. NDNS total population: *n* = 1488; female:male, 53.4%:46.6%; age range, 1.5–91 y; white:nonwhite: 91.3%:8.7%; sampled in winter, spring, summer, autumn: 24.5%, 25.9%, 24.7%, and 24.9%, respectively.

<sup>7</sup>In total, 34.0%, 27.8%, and 38.2% were of Russian-speaking, Somali, and Kurdish immigrants, respectively.

25(OH)D value for a given serum 25(OH)D value from the original method of analysis (e.g., immunoassay or LC-MS/MS) with a predefined precision of a 95% CI, as has been described elsewhere (14, 37). At the beginning of the work, once preliminary data on the current collection of population samples were available [e.g., CV of assays and spread within distribution of original serum 25(OH)D data], a projected maximum sample size of 175 sera was estimated as being sufficient to meet and, indeed, exceed the needs of the study with the highest number of sera required for standardization. Thus, for logistical considerations in dealing with multiple partner laboratories and groups within the project, all groups were requested to supply 175 stored serum samples. However, this projected maximum was confirmed as being more than sufficient for each individual study on receipt of their full existing serum 25(OH)D data files (post hoc analysis showed that sample size ranged from 60 to 155 sera being required). Regression models [ordinary least squares and Deming (weighted and unweighted) and piecewise] were used to establish the relation between the originally measured and the LC-MS/MS reanalyzed serum 25(OH)D in the subsets, as described elsewhere (14, 37). Piecewise regression is a method in regression analysis in which the independent variable is partitioned into intervals and a separate line segment is fit to each interval. A Deming regression model is an error-in-variables model that tries to find the line of best fit for a 2-dimensional data set. It differs from the simple linear regression, such as the ordinary least squares models, in that it accounts for

errors in observations on the  $x$  and  $y$  axes. We report prevalence as a yearly mean (i.e., arising from blood sampling of participants that has occurred throughout the year), as well as by extended winter and summer season, as appropriate.

## RESULTS

The relation between serum 25(OH)D in the statistical algorithm-defined subsets of serum samples from the 11 study populations, as measured by their original methods and reanalyzed by a certified LC-MS/MS method, is shown in **Table 2** and **Supplemental Figures 1 and 2**. Seven study populations (which included the NDNS “old” and “new” assay formulation subsets separately; see Supplemental Material) required a piecewise regression fit between the previously measured and LC-MS/MS remeasured serum 25(OH)D concentrations. A further 6 study populations (which included the Tromsø 6 smoker and non-smoker subsets separately) required a Deming (unweighted or weighted) regression fit between the previously measured and LC-MS/MS remeasured serum 25(OH)D concentrations. These calibration equations were applied to the entire 25(OH)D data set for the respective studies producing the standardized serum 25(OH)D data sets.

That 13.0% of the 55,844 young and adult European individuals had a yearly mean standardized serum 25(OH)D <30 nmol/L [the US Institute of Medicine’s definition of vitamin D deficiency (13)] was highlighted by the present overall pooled

**TABLE 2**

Information on the best-fit regression model between previous and newly measured 25(OH)D from subsets of serum from study populations and model coefficients<sup>1</sup>

Study ( $n$ ) <sup>2</sup> (ref)	Model type	If $Rval \leq \text{value}^3$			If $Rval > \text{value}^3$			$R^2$
		Value	Intercept 1	X1	Value	Intercept 2	X2	
HELENA (178) (15, 16)	Piecewise	69.1574	0.6266	0.9064	69.1574	41.5535	0.2965	0.76
OPUS School Meal Study (163) (17, 18)	Weighted Deming	—	1.8686	0.8921	—	—	—	0.90
Tromsø Study: Fit Futures (168) (19–21)	Weighted Deming	—	2.6488	0.7645	—	—	—	0.98
HGS (172) (22)	Weighted Deming	—	1.6027	0.6615	—	—	—	0.74
KiGGS (160) (25)	Piecewise	60.5211	9.4005	1.0225	60.5211	52.4099	0.3119	0.79
NDNS (Old) (91) <sup>4</sup> (26)	Piecewise	62.1396	4.3376	0.9719	62.1396	28.0068	0.5910	0.82
NDNS (New) (115) <sup>4</sup> (26)	Piecewise	83.5082	1.2955	1.0380	83.5082	30.3591	0.6900	0.95
DEGS (163) (27, 28)	Piecewise	121.9968	14.5309	0.7715	121.9968	102.19191	0.0529	0.79
Tromsø Study–6th Survey (nonsmokers) (168) <sup>5</sup> (29–31)	Weighted Deming	—	12.5531	0.9547	—	—	—	0.81
Tromsø Study–6th Survey (smokers) (167) <sup>5</sup> (29–31)	Unweighted Deming	—	−0.7299	0.9047	—	—	—	0.75
LASA (158) (33)	Weighted Deming	—	−2.9577	1.0375	—	—	—	0.93
AGES-Reykjavik (157) (34)	Piecewise	49.2155	7.7011	1.0128	49.2155	27.3969	0.6125	0.98
Finnish Migrant Health and Wellbeing Study (Maamu) (159) (35, 36)	Piecewise	91.8081	0.0629	1.0218	91.8081	62.7450	0.3390	0.93

<sup>1</sup>X1 and X2 are the slope(s) of the regression line(s). Three studies [Infant’s Nourishment and Nutritional Status (23), Cork BASELINE Birth Cohort Study (24), and New Hoorn Study (32)] required complete analysis of all samples as they had not previously measured serum 25(OH)D and thus were not standardized in the way the other studies were. AGES, Age, Gene/Environment Susceptibility; DEGS, German Health Interview and Examination Survey for Adults; HELENA, Healthy Lifestyle in Europe by Nutrition in Adolescence; HGS, Healthy Growth Study; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; LASA, Longitudinal Aging Study Amsterdam; NDNS, National Diet and Nutrition Survey; OPUS, Optimal well-being, development and health for Danish children through a healthy New Nordic Diet; ref, reference; 25(OH)D, 25-hydroxyvitamin D.

<sup>2</sup> $n$ , number of sera/plasma from statistical algorithm-defined subsets used for regression equation development.

<sup>3</sup>In piecewise regression, the independent variable is partitioned into intervals and a separate line segment is fit to each interval; the change point [serum 25(OH)D concentration] at which this occurs is reflected by  $Rval$  in the above equations.

<sup>4</sup>DiaSorin Liaison assay had an assay formulation change during the course of the NDNS survey, and thus “new” and “old” formulation assays are included.

<sup>5</sup>Roche ECLIA assay used in the Tromsø Study–6th Survey 6 overestimates serum 25(OH)D concentrations in smokers, and thus smokers and non-smokers are standardized separately.

estimate of 18 studies [i.e., 14 standardized in the present work plus the 4 previously standardized (14, 37)], irrespective of age group, ethnic mix, and latitude of study populations. Among those tested in the extended winter and summer periods, it was 17.7% and 8.2%, respectively. Using the alternately suggested definition of vitamin D deficiency of  $<50$  nmol/L, as per the US Endocrine Society (47), the yearly prevalence was 40.4%.

The mean, SD, median, and 5th, 25th, 75th, and 95th percentiles of serum 25(OH)D concentration using standardized serum 25(OH)D data in the childhood and teenage as well as adult and older adult study samples separately are shown in **Table 3**. The equivalent data [but based on originally analyzed serum 25(OH)D data for the 11 studies standardized in the present work] are also shown in Table 3. The prevalence estimates for serum 25(OH)D concentration below the variously proposed public health-relevant thresholds, using standardized and unstandardized serum 25(OH)D data in the childhood and teenage as well as adult and older adult study samples separately, are shown in **Table 4**. These findings highlight population subgroups within Europe at higher risk of vitamin D deficiency. Within the Finnish Maamu sample, the prevalence of serum 25(OH)D  $<30$  nmol/L was 4.5%, 28.0%, and 50.4% for white Russian-speaking, Somali, and Kurdish immigrant subgroups ( $n = 446, 364,$  and  $50$ ), respectively. Likewise, although with more limited numbers, the prevalence among the  $\sim 12\%$  non-white participants in the United Kingdom's NDNS (subset aged 1–18 y) was much higher (42.9%;  $n = 63$ ) compared with that in the equivalently aged white young individuals (15.0%,  $n = 448$ ). Because the nonwhite proportion of the populations in all other studies was  $<7\%$ , the prevalence estimates by ethnicity were not reported, but in all cases, estimates for nonwhite adult and older adults were higher compared with that of the equivalently aged white individuals within a study population (data not shown).

In general, sex differences in prevalence of serum 25(OH)D  $<30$  nmol/L within the entire collection of studies were not evident (13.1% compared with 12.9%, on average, for males and females, respectively). The prevalence of vitamin D deficiency by age group, and irrespective of latitude of study populations, suggests that teenagers may have higher risk on average. The range of deficiency in the various teenage study populations (age range: 15–18 y) was 12–40%, whereas childhood samples (age ranges: 1–6 and 7–14 y), older adult samples ( $>61$  y), and adult samples were 4–7%, 1–8%, and 9–24%, respectively (Table 4). Such comparisons need to be interpreted cautiously, because differences in latitude of sample population, ethnic mix, and season of blood sampling differed for these populations (see Table 1).

The importance of using standardized serum 25(OH)D values for comparisons of the prevalence of vitamin D deficiency is clearly illustrated by the data from 2 of the nationally representative surveys, both of which reside in a latitude band of 47–55°N. In the case of the German adult survey (German Health Interview and Examination Survey for Adults; 18–79 y), the prestandardization prevalence estimate [serum 25(OH)D  $<30$  nmol/L] of 25.9% decreased after standardization to 15.2%. For the Irish survey (National Adult Nutrition Survey), the prevalence of deficiency in adults (aged 18–84 y) increased from 6.6% (prestandardization) to 12.3% after standardization. Thus, the prevalence of vitamin D deficiency for these relatively cognate, predominantly white adult population samples, which were originally extremely disparate (25.9% compared with 6.6%),

became close after standardization (15.2% compared with 12.3%) (Table 4). The prevalence estimates for standardized serum 25(OH)D concentrations  $<30$  and  $<50$  nmol/L in the 4 nationally representative survey by extended winter and summer are also shown in **Table 5**.

## DISCUSSION

In the absence of global consensus on the concentration of 25(OH)D that defines vitamin D deficiency, the ODIN project consortium chose to use that assigned by the US Institute of Medicine [i.e.,  $<30$  nmol/L (13)], which is based on risk of metabolic bone disease. A serum 25(OH)D  $<25$  nmol/L has been a traditional cutoff used in Europe for several decades (45, 46). There is universal agreement that we do not wish to have individuals in the populations with circulating concentrations  $<25$ – $30$  nmol/L. On this basis, the present work, which is the first to report to our knowledge the prevalence estimates of vitamin D deficiency based on standardized serum 25(OH)D data, suggests that vitamin D deficiency is widespread across Europe and at prevalence rates that meet the criteria of a pandemic (definition of a pandemic: “an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people” (48). Although there was considerable variation dependent on age group, ethnic mix, and latitude of study populations, overall 13% of our combined sample of childhood, teenage, adult, and older adult population studies across Europe ( $n = 55,844$ ), ranging from southern to mid to northern European member states (35–69°N), had vitamin D deficiency (i.e.,  $<30$  nmol/L) at the time of sampling. That 13 in 100 European citizens have serum 25(OH)D concentrations  $<30$  nmol/L, using even this relatively conservative definition of vitamin D deficiency, translates into enormous numbers of individuals and highlights the need to devise strategies for prevention of vitamin D deficiency in Europe. For example, taking the vitamin D deficiency estimates of 12.5–15.2%, 12.3%, and 22.0% from the nationally representative nutrition/health surveys for Germany, Ireland, and the United Kingdom included in the present work would relate to 10.9, 0.6, and 14.1 million individuals, respectively, in these member states alone based on their recent census data. It is also worth noting that other expert bodies have suggested vitamin D deficiency is defined by a higher serum 25(OH)D threshold of 50 nmol/L (47). Using serum 25(OH)D  $<50$  nmol/L in the same surveys would translate to 44.9, 2.1, and 32.6 million individuals in Germany, Ireland, and the United Kingdom, respectively, having deficiency as defined by this threshold.

The importance of using standardized serum 25(OH)D data in the present assessment of the prevalence of vitamin D deficiency in Europe was exemplified in the upward and downward revision of prevalence estimates after standardization in some studies. For example, 10.4 million fewer German adults and 267,000 more Irish adults had vitamin D deficiency by using the estimates based on standardized compared with the corresponding non-standardized serum 25(OH)D data from these surveys. It should be stressed that standardization had very little impact on serum 25(OH)D data from a minority of population samples included in this work, which relates to the types of 25(OH)D assays used in these studies as these perform comparably to LC-MS/MS from an analytic perspective.



**TABLE 3**  
Means, SDs, medians, and 5th, 25th, 75th, and 95th percentiles of serum 25(OH)D concentrations in European populations using unstandardized and standardized data<sup>1</sup>

Study (country) (ref)	N	Serum 25(OH)D, nmol/L, via	Mean	SD	Median	Percentile			
						5th	25th	75th	95th
HELENA (9 EU countries) <sup>2</sup> (15, 16)	1006	Original	58.3	22.6	56.0	24.9	43.3	70.6	98.0
		VDSP-Calibrated	49.2 (46.8, 51.6) <sup>3</sup>	15.3 (15.3, 15.4)	50.2 (48.1, 52.2)	22.0 (18.9, 25.1)	38.5 (36.7, 40.4)	61.2 (58.5, 63.8)	71.2 (68.8, 73.6)
OPUS (baseline) (Denmark) (17, 18)	779	Original	60.8	18.7	60.0	29.9	48.0	72.2	94.5
		VDSP-Calibrated	56.1 (49.9, 62.3)	16.7 (15.6, 17.8)	55.4 (49.2, 61.5)	28.5 (24.1, 33.0)	44.7 (44.7, 50.1)	66.3 (59.4, 73.1)	86.2 (78.1, 94.2)
Tromsø Study; Fit Futures (Norway) (19–21)	939	Original	46.6	23.1	42.8	16.9	28.6	61.2	90.0
		VDSP-Calibrated	38.3 (37.1, 39.5)	17.7 (17.3, 18.0)	35.4 (34.2, 36.5)	15.6 (14.8, 16.3)	24.5 (23.6, 25.5)	49.4 (48.0, 50.9)	71.4 (69.5, 73.4)
HGS (Greece) (22)	806	Original	69.0	18.8	67.0	41.3	56.4	80.8	102.5
		VDSP-Calibrated	47.3 (39.5, 55.1)	12.5 (11.3, 13.6)	45.9 (38.2, 53.6)	28.9 (22.8, 35.1)	38.9 (31.8, 45.9)	55.1 (46.6, 63.6)	69.4 (59.6, 79.2)
INNS (Greece) (23)	215	Original	49.5	22.8	43.0	25.0	29.8	67.0	87.6
		VDSP-LC-MS/MS	54.3	15.7	54.6	30.2	43.2	65.3	79.1
Cork BASELINE Birth Cohort Study (Ireland) (24)	742	VDSP-LC-MS/MS	63.4	20.4	63.1	30.8	48.8	77.0	97.3
KiGGS <sup>4</sup> (Germany) (25)	10,015	Original	47.8	27.5	42.5	14.4	29.3	61.4	97.8
		VDSP-Calibrated	54.0 (53.7, 54.4)	19.2 (18.8, 19.7)	52.9 (52.2, 53.3)	24.1 (23.6, 24.5)	39.4 (39.0, 40.0)	71.6 (71.3, 71.8)	82.9 (82.4, 83.5)
NDNS (1–18 y) <sup>4,5</sup> (United Kingdom) (26)	511	Original	47.1	22.0	45.1	15.1	30.7	61.9	87.9
		VDSP-Calibrated	48.8 (45.8, 51.8)	19.2 (18.2, 20.3)	48.2 (45.9, 50.4)	19.0 (16.1, 21.9)	34.0 (32.1, 35.9)	64.5 (60.7, 68.2)	81.1 (73.5, 87.9)
NDNS (≥19 y) <sup>4,5</sup> (United Kingdom) (26)	977	Original	44.8	22.6	41.4	14.1	26.7	59.8	86.5
		VDSP-Calibrated	46.6 (43.6, 49.6)	20.0 (19.0, 21.1)	44.6 (42.5, 46.5)	17.7 (14.7, 20.7)	30.3 (28.2, 32.3)	62.5 (59.0, 66.1)	80.5 (73.4, 86.4)
DEGS <sup>4</sup> (Germany) (27, 28)	6995	Original	46.3	24.6	43.0	14.0	28.0	60.0	90.0
		VDSP-Calibrated	50.1 (49.6, 50.5)	18.1 (17.8, 18.4)	47.7 (46.9, 48.5)	25.3 (25.3, 26.1)	36.1 (35.4, 36.1)	60.8 (60.0, 61.6)	84.0 (82.4, 84.9)
Tromsø Study—6th Survey (Norway) (29–31)	12,817	Original	57.8	19.3	55.7	30.1	44.6	68.4	91.5
		VDSP-Calibrated	65.0 (55.2, 74.7)	17.6 (16.4, 18.9)	63.5 (54.0, 73.2)	39.1 (30.7, 47.1)	53.0 (44.3, 61.9)	74.9 (64.6, 85.1)	95.3 (83.2, 107.4)
NHS (Netherlands) (32)	2627	VDSP-LC-MS/MS	59.5	21.7	59.1	25.1	44.6	73.1	95.9
LASA (Netherlands) (33)	915	Original	65.3	21.8	63.7	32.8	49.0	79.7	103.0
		VDSP-Calibrated	64.7 (60.3, 69.2)	22.6 (21.7, 23.5)	63.1 (58.7, 67.5)	31.1 (28.0, 34.2)	47.9 (44.1, 51.7)	95.3 (74.7, 84.8)	103.9 (97.9, 109.9)
AGES—Reykjavik (Iceland) (34)	5519	Original	53.0	23.1	51.7	18.2	35.7	67.4	93.9
		VDSP-Calibrated	57.0 (53.8, 60.0)	17.8 (17.7, 17.9)	59.1 (55.9, 62.2)	26.2 (21.7, 30.6)	43.8 (41.4, 46.3)	68.8 (66.0, 71.3)	85.4 (81.2, 88.6)
Finnish Migrant Health and Wellbeing Study (Maamu) (Finland) (35, 36)	1310	Original	44.9	23.6	39.5	18.0	28.0	57.0	87.0
		VDSP-Calibrated	45.5 (43.7, 47.3)	21.9 (21.5, 22.4)	40.7 (39.4, 41.9)	18.1 (16.1, 20.0)	28.6 (27.1, 30.0)	59.1 (57.2, 60.9)	87.6 (84.4, 90.8)

<sup>1</sup>VDSP-calibrated refers to the sample standardized by the VDSP protocol with the subset reanalyzed by LC-MS/MS. In VDSP LC-MS/MS, the whole sample was analyzed by standardized LC-MS/MS. AGES, Age, Gene/Environment Susceptibility; DEGS, German Health Interview and Examination Survey for Adults; EU, European Union; HELENA, Healthy Lifestyle in Europe by Nutrition in Adolescence; HGS, Healthy Growth Study; INNS, Infant's Nourishment and Nutritional Status; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; LASA, Longitudinal Aging Study Amsterdam; LC-MS/MS, liquid chromatography–tandem mass spectrometry; NDNS, National Diet and Nutrition Survey; NHS, New Hoorn Study; OPUS, Optimal well-being, development and health for Danish children through a healthy New Nordic Diet; ref, reference; VDSP, Vitamin D Standardization Program; 25(OH)D, 25-hydroxyvitamin D.

<sup>2</sup>Greece, Spain, Italy, Hungary, Austria, France, Belgium, Germany, and Sweden.

<sup>3</sup>95% CIs on VDSP-calibrated estimates in parentheses (all such values).

<sup>4</sup>Based on unweighted estimates for comparison with other studies, weighted data are presented separately for these 4 surveys in Table 5.

<sup>5</sup>The NDNS was of individuals aged ≥1.5 y, but for this work, to allow comparison with other children and adult/older adult populations, the sample was stratified into 1–18 y and ≥19 y. NDNS total: n = 1488.



**TABLE 4**  
Prevalence of low vitamin D status in European populations using unstandardized and standardized serum 25(OH)D concentrations<sup>1</sup>

Study (country) (ref)	N	Serum 25(OH)D, nmol/L	Percentage below thresholds, nmol/L				
			<25	<30	<40	<50	<75
HELENA (9 EU countries <sup>2</sup> ) (15, 16)	1006	Original VDSP-Calibrated	4.7 7.9 (4.7, 9.6) <sup>3</sup>	9.1 12.2 (9.5, 14.7)	17.9 28.3 (24.2, 31.8)	37.3 49.4 (45.0, 53.6)	79.7 97.3 (95.7, 98.3)
OPUS (baseline) (Denmark) (17, 18)	779	Original	2.4	5.0	12.6	28.2	78.4
Tromsø Study: Fit Futures (Norway) (19–21)	939	VDSP-Calibrated	2.6 (1.4, 5.8)	6.2 (3.2, 10.1)	16.0 (10.1, 26.6)	36.8 (24.6, 52.5)	87.2 (77.5, 93.8)
HGS (Greece) (22)	806	VDSP-Calibrated	17.5	28.9	45.5	60.8	87.5
INNS (Greece) (23)	215	VDSP-Calibrated	27.3 (24.2, 29.6)	39.6 (36.4, 41.1)	59.4 (57.5, 62.5)	76.1 (73.9, 77.5)	96.0 (95.2, 96.6)
Cork BASELINE Birth Cohort Study (Ireland) (24)	742	Original	0.1	0.7	4.2	15.3	65.3
KiGGS <sup>4</sup> (Germany) (25)	10,015	VDSP-LC-MS/MS	2.2 (0.4, 9.2)	6.9 (1.6, 18.6)	28.7 (12.8, 54.7)	62.4 (40.0, 83.1)	97.4 (92.2, 99.6)
NDNS (1–18 y) <sup>4,5</sup> (United Kingdom) (26)	511	Original	1.9	25.1	42.8	59.1	86.0
NDNS (≥19 y) <sup>4,5</sup> (United Kingdom) (26)	977	VDSP-LC-MS/MS	1.4	4.2	22.3	40.5	90.2
DEGS <sup>4</sup> (Germany) (27, 28)	6995	VDSP-LC-MS/MS	1.6	4.6	14.2	26.7	74.1
Tromsø Study—6th Survey (Norway) (29–31)	12,817	Original	18.3	25.9	44.9	62.1	85.3
NHS (Netherlands) (32)	2627	VDSP-Calibrated	6.0 (5.6, 6.5)	11.9 (11.2, 12.5)	25.9 (25.0, 26.7)	44.5 (43.5, 45.5)	83.8 (83.0, 84.6)
LASA (Netherlands) (33)	915	Original	15.9	23.3	41.5	58.3	88.8
AGES—Reykjavik (Iceland) (34)	5519	VDSP-Calibrated	12.7 (9.4, 14.9)	18.4 (15.3, 21.5)	35.6 (32.1, 39.7)	53.4 (49.3, 57.7)	90.4 (87.7, 97.3)
Finnish Migrant Health and Wellbeing Study (Maamu) (Finland) (35, 36)	1310	Original	21.8	30.7	48.2	61.4	88.6
NANS <sup>4,6</sup> (Ireland) (14)	1118	VDSP-Calibrated	16.8 (12.7, 19.5)	24.0 (20.9, 28.2)	42.8 (39.6, 45.8)	57.9 (55.4, 60.7)	91.4 (87.2, 96.5)
Health 2011 <sup>6</sup> (Finland) (37)	4102	Original	19.4	28.0	44.4	60.8	88.3
HUBRO <sup>6</sup> (Norway) (37)	1042	VDSP-Calibrated	4.2 (3.8, 4.7)	12.9 (12.2, 13.7)	34.3 (33.1, 35.4)	54.5 (53.4, 55.6)	90.9 (90.2, 91.5)
Health 2006 <sup>6</sup> (Denmark) (37)	3409	Original	0.3 (0, 1.8)	0.9 (0.1, 4.4)	5.8 (1.4, 16.5)	18.6 (7.3, 39.6)	75.4 (54.3, 89.4)
		VDSP-LC-MS/MS	4.9	9.2	19.0	33.6	77.9
		Original	1.5	3.8	12.0	26.4	67.5
		VDSP-Calibrated	2.4 (1.3, 3.6)	4.6 (3.6, 6.9)	13.6 (10.2, 18.7)	28.5 (22.3, 34.3)	68.0 (60.5, 75.5)
		Original	11.3	17.2	31.2	46.9	83.3
		VDSP-Calibrated	4.2 (1.3, 7.4)	8.4 (4.6, 11.7)	19.7 (15.9, 23.0)	33.6 (30.2, 37.3)	85.8 (81.6, 89.5)
		Original	18.2	28.5	50.0	65.1	89.8
		VDSP-Calibrated	18.2 (15.5, 22.2)	28.5 (24.1, 31.3)	47.3 (45.4, 51.4)	63.7 (62.2, 65.1)	89.0 (86.5, 89.8)
		VDSP-LC-MS/MS	7.0	12.3	29.1	45.9	81.0
		VDSP-Calibrated	0.2 (0.0, 0.7)	0.4 (0.2, 0.7)	2.3 (1.6, 3.1)	6.6 (5.9, 8.9)	75.7 (70.0, 80.6)
		Original	8.9 (4.4, 12.0)	12.0 (8.9, 15.4)	19.6 (17.0, 21.7)	27.9 (24.0, 31.3)	65.6 (59.9, 71.7)
		VDSP-Calibrated	0 (0, 4.8)	4.3 (0, 7.3)	10.9 (6.8, 15.5)	23.6 (18.3, 28.7)	67.7 (61.5, 73.7)

<sup>1</sup>VDSP-calibrated refers to the sample standardized by the VDSP protocol with the subset reanalyzed by LC-MS/MS. In VDSP LC-MS/MS, the whole sample was analyzed by standardized LC-MS/MS. AGES, Age, Gene/Environment Susceptibility; DEGS, German Health Interview and Examination Survey for Adults; EU, European Union; HELENA, Healthy Lifestyle in Europe by Nutrition in Adolescence; HGS, Healthy Growth Study; HUBRO, Oslo Health Study; INNS, Infant's Nourishment and Nutritional Status; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; LASA, Longitudinal Aging Study Amsterdam; LC-MS/MS, liquid chromatography–tandem mass spectrometry; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NHS, New Hoor Study; OPUS, Optimal well-being, development and health for Danish children through a healthy New Nordic Diet; ref, reference; VDSP, Vitamin D Standardization Program; 25(OH)D, 25-hydroxyvitamin D. <sup>2</sup>Greece, Spain, Italy, Hungary, Austria, France, Belgium, Germany, and Sweden.

<sup>3</sup>95% CIs on VDSP-calibrated estimates in parentheses (all such values).

<sup>4</sup>Based on unweighted estimates for comparison with other studies, weighted data are presented separately for these 4 surveys in Table 5.

<sup>5</sup>The NDNS was of individuals aged ≥1.5 y, but for this work, to allow comparison with other children and adult/older adult populations, the sample was stratified into 1–18 and >19 y. NDNS total: n = 1488, original and standardized percent <30 nmol/L, 28.2% and 22.0%, respectively.

<sup>6</sup>Data from previous standardized studies (14, 37) included for information and comparison purposes.

**TABLE 5**

Prevalence of standardized serum 25(OH)D concentrations <30 and <50 nmol/L for 4 national nutritional/health surveys based on weighted data, stratified by extended winter and summer<sup>1</sup>

Study (country; <i>n</i> ) (ref)	% Serum 25(OH)D <30 nmol/L			% Serum 25(OH)D <50 nmol/L		
	Yearly	Extended winter	Extended summer	Yearly	Extended winter	Extended summer
KiGGS (Germany; <i>n</i> = 10,015) (25)	12.5	21.1	5.7	45.6	64.3	30.7
DEGS (Germany; <i>n</i> = 6995) (27, 28)	15.2	25.5	6.9	56.0	74.9	40.7
NDNS: Rolling Program Year 1–4 (United Kingdom; <i>n</i> = 1488) (26)	22.1	31.8	15.3	55.4	69.3	45.7
NANS (Ireland; <i>n</i> = 1118) (14)	12.4	19.7	6.6	46.0	61.2	35.4

<sup>1</sup>Extended winter: November–March; extended summer: April–October. Values are based on weighted estimates. DEGS, German Health Interview and Examination Survey for Adults; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; ref, reference; 25(OH)D, 25-hydroxyvitamin D.

As expected, there was considerable variation in prevalence of vitamin D deficiency among the European Union countries, which appeared to be dependent on age group. In studies of adult and older adult populations, the prevalence of vitamin D deficiency was much less in the more northerly latitude countries such as Norway, Iceland, and Finland, whereas more mid-latitude countries such as the United Kingdom, Ireland, Netherlands, and Germany had a higher prevalence, even accounting for ethnicity. The amplitude of an increase in prevalence in vitamin D deficiency in extended winter compared with extended summer was also much lower in the northerly latitude countries, which is likely attributable to higher rates of vitamin D supplement and/or food fortification use in these countries (49–51). In the case of the childhood population studies, the relatively mid-latitude countries (47–60°N) had a higher prevalence range (5–20%) than did southern countries (<41°N) at 4.2–6.9%.

The present findings may also be of importance to risk managers in the European Commission and the various member states within Europe as they highlight population subgroups within Europe that may be at increased risk of vitamin D deficiency and that may require a specific focus on devising public health strategies for the prevention of deficiency. Nonwhite populations in Europe are at higher risk of vitamin D deficiency than their white counterparts. For example, compared with white populations in the United Kingdom, Norway, and Finland, the nonwhite population subgroups have 3- to 71-fold higher yearly prevalence of vitamin D deficiency. Differences also exist within different nonwhite ethnic groups residing in the same country. For example, within the Finnish Maamu representative sample, the Kurdish immigrant subgroup (*n* = 500) had a much higher prevalence of yearly serum 25(OH)D <30 nmol/L (50.4%) than the Somali immigrant subgroup (28.0%; *n* = 364), and both were much higher than either the Russian-speaking white immigrant subgroup (4.5%; *n* = 446) in Maamu or the general Finnish native white adult population as studied in the representative Health 2011 survey (37) (0.4%; *n* = 4102). Although not assessed in the present analysis, the subjects of Kurdish origin (born in Iraq or Iran) in the present study generally have, on average, a lighter skin pigmentation than those of Somali origin, highlighting that skin color is only part of the reason for lower vitamin D status in certain ethnic groups and that other (dietary, cultural, and biologic) factors influence the prevalence of vitamin D deficiency. As an additional insight, although cognizant of the fact that the numbers were low and thus caution is needed in their interpretation, the current analysis of standardized serum

25(OH)D from the United Kingdom's NDNS (all subjects) showed that the prevalence of vitamin D deficiency was 35.7% and 59.6% in black (*n* = 28) and Asian participants (*n* = 52), respectively, compared with 19.6% in white participants (*n* = 1359). Standardized serum 25(OH)D data for South Asian (Pakistani) immigrants in Oslo, Norway, also highlight an extremely high prevalence of vitamin D deficiency (64.8%, *n* = 176) relative to that in the white native adult population (1.3%, *n* = 866) (37). European teenagers, aged 15–18 y, seemed to exhibit a higher prevalence of vitamin D deficiency (range: 12.2–39.6%) than did other age groups (range: 0.9–19.6%), a phenomenon observed previously (52–54). It is worth noting that none of the studies included pregnant women or older adults in care homes, both life-stage groups that are considered vulnerable to vitamin D deficiency. In general, sex differences in the prevalence of vitamin D deficiency within the collection of population studies were not very pronounced compared with ethnic and some age-grouping differences. Thus, risk of vitamin D deficiency was largely similar in males and females of both young and older European populations.

The key strengths of this study were the inclusion of the 18 representative European population studies of children, teenagers, adults, and older adults, representing a sizable geographical footprint with 55,844 total participants, and our ability to standardize their serum 25(OH)D data so as to better quantify the prevalence of vitamin D deficiency in Europe and inform development of prevention policies. In terms of limitations of this study, it is worth noting that some of the studies were 7–11 y old, and vitamin D supplement and/or fortified food usage patterns and formulations as well as adherence to sun awareness campaigns since that time may have altered, which would affect these estimates.

In conclusion, vitamin D deficiency is evident throughout the European population at prevalence rates that are a matter of concern and that require action both from a public health and a clinical perspective. What direction these strategies take will depend on risk managers. Although there have been some guidelines on sun exposure (55), the question of whether a minimal-risk approach to UV-B exposure would enable vitamin D production without increasing the risk of skin cancer is still outstanding. It is the view of this consortium that these factors re-emphasize the need for public health strategies to explore food-based solutions for prevention of vitamin D deficiency. The pros and cons of vitamin D supplementation and/or food fortification have been well documented in recent times (49, 56–58). Finally,



assessment of the prevalence of vitamin D deficiency within and between populations is enormously enhanced by use of standardized serum 25(OH)D data.

The following authors were the link and designated principal investigators within the ODIN project consortium and who provided sera and required data on each of their various population studies, as follows: Healthy Lifestyle in Europe by Nutrition in Adolescence: M González-Gross, J Valtueña, S De Henauw, and L Moreno; Optimal well-being, development and health for Danish children through a healthy New Nordic Diet: CT Damsgaard, KF Michaelsen, and C Mølgaard; Tromsø 6 and Fit Futures: R Jorde and G Grimnes Infant's Nourishment and Nutritional Status and Healthy Growth Study: G Moschonis, C Mavrogianni, and Y Manios; German Health Interview and Examination Survey for Children and Adolescents and German Health Interview and Examination Survey for Adults: M Thamm, GBM Mensink, M Rabenberg, and MA Busch; NDNS: L Cox, S Meadows, G Goldberg, and A Prentice; New Hoorn Study: JM Dekker, G Nijpels, and S Pilz; Longitudinal Aging Study Amsterdam: KM Swart, NM van Schoor, and P Lips; Age, Gene/Environment Susceptibility-Reykjavik: G Eiriksdottir, V Gudnason, and MF Cotch; Maamu: S Koskinen and C Lamberg-Allardt; Cork BASELINE: M Kiely.

We thank Nida Ziauddeen from the MRC Human Nutrition Research Unit and Elsie Widdowson Laboratory, Cambridge, United Kingdom, for her help with calculating the weighted estimates for the NDNS data.

The authors' responsibilities were as follows—MG-G, JV, SDH, LM, CTD, KFM, C Mølgaard, RJ, G Grimnes, GM, C Mavrogianni, YM, MT, GBMM, MR, MAB, LC, SM, G Goldberg, AP, JMD, GN, SP, KMS, NMvS, PL, GE, VG, MFC, SK, CL-A, and MK: supplied sera and data on the population studies to allow standardization of serum 25(OH)D; KGD, ZŠ, and SM: undertook the LC-MS/MS analysis and associated data analysis; KDC, RAD-A, and CTS: performed regression modeling and statistical analysis; KDC and MK: were ODIN project coordinators; and KDC: drafted the manuscript. The authors declared no conflicts of interest.

## REFERENCES

- Holick MF. The vitamin D deficiency pandemic and consequences for nonskeletal health: mechanisms of action. *Mol Aspects Med* 2008;29:361–8.
- Grant WB, Cross HS, Garland CF, Gorham ED, Moan J, Peterlik M, Porojnicu AC, Reichrath J, Zittermann A. Estimated benefit of increased vitamin D status in reducing the economic burden of disease in western Europe. *Prog Biophys Mol Biol* 2009;99:104–13.
- Seamans KM, Cashman KD. Existing and potentially novel functional markers of vitamin D status: a systematic review. *Am J Clin Nutr* 2009;89:1997S–2008S.
- Sempos CT, Vesper HW, Phinney KW, Thienpont LM, Coates PM. Vitamin D status as an international issue: national surveys and the problem of standardization. *Scand J Clin Lab Invest Suppl* 2012;243:32–40.
- Cashman KD, Kiely M. Towards prevention of vitamin D deficiency and beyond—knowledge gaps and research needs in vitamin D nutrition and public health. *Br J Nutr* 2011;106:1617–27.
- Hilger J, Friedel A, Herr R, Rausch T, Roos F, Wahl DA, Pierroz DD, Weber P, Hoffmann K. A systematic review of vitamin D status in populations worldwide. *Br J Nutr* 2014;111:23–45.
- Binkley N, Krueger D, Cowgill CS, Plum L, Lake E, Hansen KE, DeLuca HF, Drezner MK. Assay variation confounds the diagnosis of hypovitaminosis D: a call for standardization. *J Clin Endocrinol Metab* 2004;89:3152–7.
- Carter GD, Carter R, Jones J, Berry J. How accurate are assays for 25-hydroxyvitamin D? Data from the international vitamin D external quality assessment scheme. *Clin Chem* 2004;50:2195–7.
- Carter GD. 25-Hydroxyvitamin D: a difficult analyte. *Clin Chem* 2012;58:486–8.
- Lai JK, Lucas RM, Banks E, Posonby AL; Ausimmune Investigator Group. Variability in vitamin D assays impairs clinical assessment of vitamin D status. *Intern Med J* 2012;42:43–50.
- van Schoor NM, Lips P. Worldwide vitamin D status. *Best Pract Res Clin Endocrinol Metab* 2011;25:671–80.
- Binkley N, Sempos CT, for the Vitamin D Standardization Program (VDSPP). Standardizing vitamin D assays: the way forward. *J Bone Miner Res* 2014;29:1709–14.
- Institute of Medicine Food and Nutrition Board. Dietary reference intakes for calcium and vitamin D. Washington (DC): National Academies Press; 2011.
- Cashman KD, Kiely M, Kinsella M, Durazo-Arvizu RA, Tian L, Zhang Y, Lucey A, Flynn A, Gibney MJ, Vesper HW, et al. Evaluation of Vitamin D Standardization Program protocols for standardizing serum 25-hydroxyvitamin D data: a case study of the program's potential for national nutrition and health surveys. *Am J Clin Nutr* 2013;97:1235–42.
- Moreno LA, De Henauw S, González-Gross M, Kersting M, Molnár D, Gottrand F, Barrios L, Sjöström M, Manios Y, Gilbert CC, et al. Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. *Int J Obes (Lond)* 2008;32:S4–11.
- González-Gross M, Valtueña J, Breidenassel C, Moreno LA, Ferrari M, Kersting M, De Henauw S, Gottrand F, Azzini E, Widhalm K, et al. Vitamin D status among adolescents in Europe: the Healthy Lifestyle in Europe by Nutrition in Adolescence study. *Br J Nutr* 2012;107:755–64.
- Damsgaard CT, Dalskov SM, Petersen RA, Sørensen LB, Mølgaard C, Biloft-Jensen A, Andersen R, Thorsen AV, Tetens I, Sjödin A, et al. Design of the OPUS School Meal Study: a randomised controlled trial assessing the impact of serving school meals based on the New Nordic Diet. *Scand J Public Health* 2012;40:693–703.
- Damsgaard CT, Dalskov SM, Laursen RP, Ritz C, Hjorth MF, Lauritzen L, Sørensen LB, Petersen RA, Andersen MR, Stender S, et al. Provision of healthy school meals does not affect the metabolic syndrome score in 8-11-year-old children, but reduces cardiometabolic risk markers despite increasing waist circumference. *Br J Nutr* 2014;112:1826–36.
- The Tromsø Study [Internet]. [cited 2013 Oct 22]. Tromsø (Norway): UiT The Arctic University of Norway; 2015. Available from: <http://www.tromsostudy.com>.
- Winther A, Dennison E, Ahmed LA, Furberg AS, Grimnes G, Jorde R, Gjesdal CG, Emaus N. The Tromsø Study: Fit Futures: a study of Norwegian adolescents' lifestyle and bone health. *Arch Osteoporos* 2014;9:185.
- Oberg J, Jorde R, Almås B, Emaus N, Grimnes G. Vitamin D deficiency and lifestyle risk factors in a Norwegian adolescent population. *Scand J Public Health* 2014;42:593–602.
- Moschonis G, Tanagra S, Vandrova A, Kyriakou AE, Dede V, Siatitsa PE, Koumpitski A, Androutsos O, Grammatikaki E, Kantilafti M, et al. Social, economic and demographic correlates of overweight and obesity in primary-school children: preliminary data from the Healthy Growth Study. *Public Health Nutr* 2010;13:1693–700.
- McBride D, Keil T, Grabenhenrich L, Dubakiene R, Drasutiene G, Fiocchi A, Dahdah L, Sprickelman AB, Schoemaker AA, Roberts G, et al. The EuroPrevall birth cohort study on food allergy: baseline characteristics of 12,000 newborns and their families from nine European countries. *Pediatr Allergy Immunol* 2012;23:230–9.
- O'Donovan SM, Murray DM, Hourihane JO, Kenny LC, Irvine AD, Kiely M. Cohort profile: The Cork BASELINE Birth Cohort Study: Babies after SCOPE: Evaluating the Longitudinal Impact on Neurological and Nutritional Endpoints. *Int J Epidemiol* 2015.
- Kurth BM, Kamtsiuris P, Hölling H, Schlaud M, Dölle R, Ellert U, Kahl H, Knopf H, Lange M, Mensink GB, et al. The challenge of comprehensively mapping children's health in a nation-wide health survey: design of the German KiGGS-Study. *BMC Public Health* 2008;8:196.
- National Diet and Nutrition Survey [Internet]. Results from years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012). [cited 2015 Mar 1]. London: Public Health London; 2014. Available from: <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>.
- Scheidt-Nave C, Kamtsiuris P, Göbbwald A, Hölling H, Lange M, Busch MA, Dahm S, Dölle R, Ellert U, Fuchs J, et al. German health interview and examination survey for adults (DEGS)—design, objectives and implementation of the first data collection wave. *BMC Public Health* 2012;12:730.
- Kamtsiuris P, Lange M, Hoffmann R, Schaffrath Rosario A, Dahm S, Kuhnert R, Kurth BM. The first wave of the German Health Interview and Examination Survey for Adults (DEGS1): sampling design, response, sample weights and representativeness. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2013;56:620–30.

29. Jacobsen BK, Eggen AE, Mathiesen EB, Wilsgaard T, Njølstad I. Cohort profile: the Tromso Study. *Int J Epidemiol* 2012;41:961–7.
30. Eggen AE, Mathiesen EB, Wilsgaard T, Jacobsen BK, Njølstad I. The sixth survey of the Tromso Study (Tromso 6) in 2007–08: collaborative research in the interface between clinical medicine and epidemiology: study objectives, design, data collection procedures, and attendance in a multipurpose population-based health survey. *Scand J Public Health* 2013;41:65–80.
31. Grimnes G, Almaas B, Eggen AE, Emaus N, Figenschau Y, Hopstock LA, Hutchinson MS, Methlie P, Mihailova A, Sneve M, et al. Effect of smoking on the serum levels of 25-hydroxyvitamin D depends on the assay employed. *Eur J Endocrinol* 2010;163:339–48.
32. van 't Riet E, Alsema M, Rijkeltijkhuizen JM, Kostense PJ, Nijpels G, Dekker JM. Relationship between A1C and glucose levels in the general Dutch population: the new Hoorn study. *Diabetes Care* 2010;33:61–6.
33. Huisman M, Poppelaars J, van der Horst M, Beekman AT, Brug J, van Tilburg TG, Deeg DJ. Cohort profile: the Longitudinal Aging Study Amsterdam. *Int J Epidemiol* 2011;40:868–76.
34. Harris TB, Launer LJ, Eiriksdottir G, Kjartansson O, Jonsson PV, Sigurdsson G, Thorgeirsson G, Aspelund T, Garcia ME, Cotch MF, et al. Age, Gene/Environment Susceptibility–Reykjavik Study: multi-disciplinary applied phenomics. *Am J Epidemiol* 2007;165:1076–87.
35. Migrant Health and Wellbeing Study (Maamu). [cited 2015 Mar 1]. Helsinki (Finland): National Institute for Health and Welfare; 2015. Available from: <https://www.thl.fi/fi/web/thlfi-en/research-and-expertwork/population-studies/migrant-health-and-wellbeing-study-maamu>.
36. Tiittala PJ, Kivelä PS, Ristola MA, Surcel HM, Koponen PM, Mölsä M, Ollgren J, Liitsola K. Maamu HIV paper: achieving high acceptability of HIV testing in a population-based survey among immigrants in Finland. *Scand J Public Health* 2015;43:393–8.
37. Cashman KD, Dowling KG, Škrabáková Z, Kiely M, Lamberg-Allardt C, Durazo-Arvizu RA, Sempos CT, Koskinen S, Lundqvist A, Sundvall J, et al. Standardizing serum 25-hydroxyvitamin D data from four Nordic population samples using the Vitamin D Standardization Program protocols: shedding new light on vitamin D status in Nordic individuals. *Scand J Clin Lab Invest* 2015;75:549–61.
38. Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. *J Clin Endocrinol Metab* 1988;67:373–8.
39. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA). Scientific opinion on principles for deriving and applying Dietary Reference Values. *EFSA J* 2010;8:1458.
40. Tian L, Durazo-Arvizu RA, Myers G, Brooks S, Sarafin K, Sempos CT. The estimation of calibration equations for variables with heteroscedastic measurement errors. *Stat Med* 2014;33:4420–36.
41. Rahmani YE, Botelho JC & Vesper HW. CDC Vitamin D Standardization Certification Program. *Endocr Rev* 2013;34:SUN-277.
42. Ellis G, Dixon K. Sequential-saturation-type assay for serum 25-hydroxyvitamin D. *Clin Chem* 1977;23:855–62.
43. Antonucci DM, Black DM, Sellmeyer DE. Serum 25-hydroxyvitamin D is unaffected by multiple freeze-thaw cycles. *Clin Chem* 2005;51:258–61.
44. Hollis BW. Measuring 25-hydroxyvitamin D in a clinical environment: challenges and needs. *Am J Clin Nutr* 2008;88:507S–10S.
45. Department of Health. Dietary reference values for food energy and nutrients for the United Kingdom. London: Her Majesty's Stationery Office; 1991. (Report on Health and Social Subjects 41.)
46. Commission of the European Communities. Vitamin D. In: Nutrient and energy intakes of the European Community: report of the Scientific Committee for Food. 31st series. Brussels (Luxembourg): Office of Official Publications of the European Communities; 1993. p. 132–9.
47. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011;96:1911–30.
48. Last J. A dictionary of epidemiology. 4th ed. Oxford (United Kingdom): Oxford University Press; 2001.
49. Kiely M, Black LJ. Dietary strategies to maintain adequacy of circulating 25-hydroxyvitamin D concentrations. *Scand J Clin Lab Invest Suppl* 2012;243:14–23.
50. Norwegian Directorate of Health, Norwegian Food Safety Authority and University of Oslo. Norkost 3: a nationwide dietary survey among men and women in Norway aged 18–70 years. Oslo: Norwegian Directorate of Health; June 2012. (Report IS-2000.)
51. Helldán A, Raulio S, Kosola M, Tapanainen H, Ovaskainen M-L, Virtanen S. Finravinto 2012–tutkimus—The National FINDIET 2012 Survey. Raportti 16/2013. Helsinki (Finland): National Institute for Health and Welfare; 2013.
52. Cashman KD. Vitamin D in childhood and adolescence. *Postgrad Med J* 2007;83:230–5.
53. Guillemant J, Taouin P, Le HT, Taright N, Allemandou A, Pérès G, Guillemant S. Vitamin D status during puberty in French healthy male adolescents. *Osteoporos Int* 1999;10:222–5.
54. Ginty F, Cavadini C, Michaud P-A, Burckhardt P, Baumgartner M, Mishra GD, Barclay DV. Effects of usual nutrient intake and vitamin D status on markers of bone turnover in Swiss adolescents. *Eur J Clin Nutr* 2004;58:1257–65.
55. National Institute for Health and Care Excellence. Sunlight exposure: communicating the benefits and risks to the general public—draft guideline [Internet]. [cited 2015 Jun 30]. London: National Institute for Health and Care Excellence; 2015. Available from: <http://www.nice.org.uk/guidance/gid-phg77/resources/sunlight-exposure-benefits-and-risks-draft-guideline2>.
56. Black LJ, Walton J, Flynn A, Cashman KD, Kiely M. Small increments in vitamin D intake by Irish adults over a decade show that strategic initiatives to fortify the food supply are needed. *J Nutr* 2015;145:969–76.
57. Cashman KD. Vitamin D: dietary requirements and food fortification as a means of helping achieve adequate vitamin D status. *J Steroid Biochem Mol Biol* 2015;148:19–26.
58. Allen RE, Dangour AD, Tedstone AE, Chalabi Z. Does fortification of staple foods improve vitamin D intakes and status of groups at risk of deficiency? A United Kingdom modeling study. *Am J Clin Nutr* 2015;102:338–44.

