Prediction of vitamin D deficiency by simple patient characteristics1–3

Evelien Sohl, Martijn W Heymans, Renate T de Jongh, Martin den Heijer, Marjolein Visser, Thomas Merlin, Paul Lips, and Natasja M van Schoor

ABSTRACT
Background: Vitamin D status is currently diagnosed by measuring serum 25-hydroxyvitamin D [25(OH)D].
Objective: This study aimed to develop a risk profile that can be used to easily identify older individuals at high risk of vitamin D deficiency.
Design: This study was performed within the Longitudinal Aging Study Amsterdam, an ongoing cohort study in a representative sample of the Dutch older population (n = 1509 for the development sample and n = 1100 for the validation sample). Prediction models for serum 25(OH)D concentrations <50 and <30 nmol/L were developed by using backward logistic regression. Risk scores were calculated by dividing the individual regression coefficients by the regression coefficient with the lowest β to create simple scores.
Results: Serum 25(OH)D concentrations <50 and <30 nmol/L were present in 46.2% and 17.5% of participants, respectively. The model for the prediction of concentrations <50 nmol/L consisted of 13 easily assessable predictors, whereas the model for concentrations <30 nmol/L contained 10 predictors. The resulting areas under the curve (AUCs) were 0.78 and 0.80, respectively. The AUC in the external validation data set was 0.71 for the <50-nmol/L model. At a cutoff of 58 in total risk score (range: 8–97), the model predicted concentrations <50 nmol/L with a sensitivity of 61% and a specificity of 82%, whereas these values were 61% and 84%, respectively, at a cutoff of 110 in the total risk score (range: 6–204) in the model for concentrations <30 nmol/L.
Conclusions: Two total risk scores, including 13 or 10 predictors that can easily be assessed, were developed and are able to predict serum 25(OH)D concentrations <50 and <30 nmol/L accurately. These risk scores may be useful in clinical practice to identify persons at risk of vitamin D deficiency.

INTRODUCTION
Vitamin D deficiency is common in older individuals (1). Depending on the definition used for deficiency, age, sex, lifestyle, and season and the method used for determination, the percentage of individuals with deficiency ranges from 50% to 90% (1, 2). Vitamin D is essential for bone health; older individuals with vitamin D deficiency have a higher risk of falls and fractures (3). In addition, vitamin D has been proposed to play a role in the development of many other disorders, such as cancer, diabetes, autoimmune disease, and infections, and poorer cognitive function (4–7). However, the effects on most outcomes remain to be proven by randomized controlled trials.

The Institute of Medicine (IOM)2 advises extra supplementation in all older individuals to obtain the recommended serum 25-hydroxyvitamin D [25(OH)D] concentration of 30–50 nmol/L (8). Recent advice from the Dutch Health Council also states that all men and women >70 y of age should take a supplement of 20 μg vitamin D/d and all women aged ≥50 y are advised to take 10 μg vitamin D/d to obtain the recommended 25(OH)D concentration of 50 nmol/L (9). However, only ~50% of individuals aged ≥65 y in the Netherlands has vitamin D deficiency (<50 nmol/L) according to the results of the Longitudinal Aging Study Amsterdam (LASA) (10) and those of the Hamlet study (11). This suggests that 50% of the population aged ≥65 y take vitamin D supplements that may not be necessary.

The number of laboratory requests for the determination of serum 25(OH)D is increasing as a consequence of the proposed influence of vitamin D on many organs and diseases (12). This contributes to an increase in health care costs (13). It would be useful to have a model to predict vitamin D deficiency reliably and therefore to identify individuals who could benefit from vitamin D supplementation without the need to determine their 25(OH)D status.

Recently, a model for the prediction of vitamin D deficiency in Australian individuals was published (14). However, an adequate model in European individuals does not exist. To decrease the costs of laboratory tests and the number of people who unnecessarily use vitamin D supplements, this study aimed to develop 2 prediction models for determining serum 25(OH)D <50 nmol/L as well as concentrations <30 nmol/L. To make these models easy to use in daily practice, only easily assessable predictors were included.

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2 An unconditional grant was received from Merck & Co for part of the vitamin D measurements. This study was partly funded by ZonMw. The Longitudinal Aging Study Amsterdam is largely supported by a grant from The Netherlands Ministry of Health, Welfare, and Sports, Directorate of Long-Term Care.
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4 Abbreviations used: IOM, Institute of Medicine; LASA, Longitudinal Aging Study Amsterdam; 25(OH)D, 25-hydroxyvitamin D.
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SUBJECTS AND METHODS

Study sample

Data for this study were derived from LASA. LASA is an ongoing cohort study in a representative sample of the Dutch older population. The sampling and data collection procedures have been described elsewhere in detail (15, 16). Briefly, a random sample of men and women, stratified by age, sex, and expected 5-y mortality rate, was drawn from population registers from 11 municipalities in the Netherlands. At baseline (1992/1993), 3,107 subjects aged 55–85 y were interviewed. In 2002, a second cohort, consisting of 1,002 individuals aged 55–65 y, was recruited. After the 2002 measurement cycle, both cohorts were combined in subsequent measurement cycles. The study was approved by the Medical Ethics Committee of the VU University Medical Center, and all participants gave informed consent.

For the present study, the second measurement cycle of the first cohort (1995/1996) was used. In the first cohort, persons who participated in the medical interview in addition to the main interview in 1995/1996 and who were born in or before 1930 (aged ≥65 y as of 1 January 1996) were selected (n = 1,509).

For the external validation of the model, we used the 2008/2009 measurement cycle of the first and second cohorts combined (ages 61–95 y). Individuals of the first cohort, who were already in the sample for the development of our models, were excluded. For the validation sample, we included the participants in the medical interview (n = 1,100).

Serum 25(OH)D

Morning blood samples were drawn in 1995/1996 and in 2008/2009. In 1995/1996, the participants were allowed to consume tea and toast but no dairy products, whereas participants in 2008/2009 fasted from midnight until after morning blood collection. The samples were centrifuged and stored at −20°C until determination in 1997/1998 or 2010/2011, respectively. For both analyses, a competitive binding protein assay was used (1997/1998: Nichols Diagnostics; 2010/2011: Diasorin). The interassay CVs were <10% for both methods. Both methods were compared by measuring 117 samples (41 LASA participants and 76 samples measured for clinical purposes) with both methods. These analyses showed that concentrations of 25, 50, and 75 nmol/L, measured with the Nichols assay equaled 31.1, 54.2, and 77.2 nmol/L, respectively, when measured with the Diasorin assay. The correlation coefficient was r = 0.94. For this study, original values were used. All analyses were performed in the Endocrine Laboratory of the VU University Medical Center.

Potential predictors

The following potential predictors were included in the analyses: age, sex, BMI (in kg/m²), smoking, alcohol use, level of education, season, vitamin use, physical activity (bicycling, walking, sports, gardening), degree of urbanization, medication use, self-rated health, specific depressive symptoms, anxiety, functional limitations, partner status, pain during walking, memory complaints, and some specific items from the Mini Mental State Examination. Predictors that were included in the final models (see Table 2) are described in more detail below (detailed information on all potential predictors is available as Supplemental Material under “Supplemental data” in the online issue).

Age and sex were derived from population registries. BMI was calculated as measured weight in kilograms divided by measured height in square meters. Self-reported smoking was divided into 2 categories: current smoker (including participants who stopped smoking within the past 5 y) and nonsmoker. Alcohol use was assessed by self-report. Season was categorized into 4 categories according to the meteorologic seasons in the Netherlands (winter: December–February; spring: March–May; summer: June–August; and autumn: September–November). Over-the-counter vitamin use was based on self-report (yes or no). These multivitamin tablets typically contain 200–400 IU vitamin D. Physical activity was assessed by using the LASA Physical Activity Questionnaire, a validated interviewer-administered questionnaire (17). For this study, only the first question on every domain (eg, “Do you walk outdoors?”) was used. For gardening, if participants did not have a garden, they were classified as “no gardening.” Medication use was assessed by asking the participants to show their medication containers to the interviewers; a dichotomization was made into no medication use or the use of one or more medicines. Participants’ inability to use their own or public transportation was assessed by asking a question on the ability to perform this activity. Partner status was divided into 2 categories: having a partner or no partner. The Mini-Mental State Examination assessed whether a participant knew the current year (18). The presence of appetite was assessed by using a question from the Center for Epidemiologic Studies–Depression scale questionnaire (19).

Statistical analyses

Cutoffs for vitamin D concentrations were determined at serum 25(OH)D concentrations <50 and <30 nmol/L, according to the guidelines from the IOM and those from the Dutch Health Council (8, 9). The IOM states that concentrations <30 nmol/L increase the risk of deficiency with regard to bone health and that concentrations between 30 and 50 nmol/L indicate an increased risk of inadequacy for some, but not all, individuals (8). The Dutch Health Council has set the recommended serum 25(OH)D concentrations at 30 nmol/L for adults and at 50 nmol/L for women aged >50 y and for men >70 y (9).

All continuous variables were tested for linearity by using spline curves and spline regression models (20). When linearity was not present, the variable was categorized or dichotomized mainly according to known cutoffs derived from the literature. To determine the optimal cutoffs of continuous variables that needed to be categorized, different known cutoffs were tested and the cutoff with the highest predictive value was selected. Age was used as a continuous variable; all ages were centered at 65 y. BMI was dichotomized into nonobese (<30) and obese (≥30). Alcohol use was dichotomized as ≤12 or >12 drinks/wk.

The univariable ORs of the observed data were calculated by using logistic regression analyses. Multiple imputation of missing values was performed for participants in the medical interview (n = 1,509). Multiple imputations were generated by using the Multivariate Imputation by Chained Equations procedure (21). With this regression-based method, missing values are estimated by using an imputation model including information from other complete
variables in the data set. We created 27 different imputed data sets according to the percentage of missing cases in the multivariable models (22).

To select predictors that could be used in the model to identify individuals at risk of vitamin D deficiency, we used a backward selection procedure within the logistic regression analyses and taking into account the imputed data sets (23). The selection criterion was \( P < 0.157 \), Akaike’s information criterion (24).

First, all potential predictors were included in the model; second, the predictor with the highest \( P \) value was excluded from the model. This was done until all remaining predictors had a \( P \) value lower than the predefined selection criterion. The probability of being vitamin D deficient was calculated by using the following formula:

\[
P_{\text{deficient}} = \frac{e^{(b_0 + b_1 x_1 + b_2 x_2 + \ldots + b_n x_n)}}{1 + e^{(b_0 + b_1 x_1 + b_2 x_2 + \ldots + b_n x_n)}}
\]

where \( P \) is the probability of being vitamin D deficient, \( b_0 \) is the constant and \( b_1, b_2, \ldots, b_n \) represent the regression coefficient of the predictors \( x_1, x_2, \ldots, x_n \) after they were pooled using Rubin’s rules. By using these predicted probabilities, a receiver operator characteristic curve was made. The goodness-of-fit of the model was tested by the Hosmer-Lemeshow test (25). Internal validation of the model was determined by using bootstrapping techniques, which provide information about the performance of the model in comparable patient data sets. On the basis of this information, regression coefficients and performance measures were adjusted (26).

The regression coefficients of the predictors in the pooled model were divided by the regression coefficient of the predictor with the lowest \( \beta \) to calculate individual risk scores. These individual scores can be summed to calculate the total risk score. The sensitivity, specificity, and positive and negative predictive values of the total risk score were calculated. Specificity is defined as the proportion of individuals who are not deficient and who are correctly classified as nondeficient. Sensitivity is the proportion of individuals who are deficient and who are correctly classified as deficient.

External validation was performed by calculating the AUC in the validation sample by using the internally validated regression coefficients. Missing values in the external validation sample were imputed by using the same procedure as was performed in the development sample. The analyses were performed by using SPSS for Windows, version 20 (SPSS, Inc), and R, version 2.15.0 (R Project for Statistical Computing).

**RESULTS**

Among the 1509 participants in the 1995/1996 medical interview, 1106 had complete data on all potential predictors. Mean (±SD) serum 25(OH)D was 53.2 ± 24.0 nmol/L. Serum 25(OH)D concentrations <50 nmol/L were present in 46.2% of the participants and 25(OH)D concentrations <30 nmol/L were present in 17.5% of the participants. The prevalence and the univariable ORs for serum 25(OH)D concentrations <50 and <30 nmol/L for the observed nonimputed data (\( n = 1106 \)) are presented in Table 1.

By using a backward selection procedure, the final prediction model for serum 25(OH)D <50 nmol/L consisted of the following variables: older age, sex (female), BMI (>30), smoking, alcohol consumption (<13 drinks/wk), season, no vitamin supplement use, no bicycling, no sporting, no gardening, medication use, poor appetite, and without a partner (Table 2). The probability of vitamin D deficiency for a 65-y-old participant ranged from 2% when none of the predictors was present to 85% when all of the predictors were present. For an 80-y-old participant, the respective probabilities of being vitamin D deficient ranged from 6% to 94%. The Hosmer-Lemeshow goodness-of-fit test for the multiple logistic regression was not significant, which indicates that the model fit the data well. After internal validation, the resulting AUC was 0.78. Nagelkerke’s \( R^2 \) was 0.31. When the model was validated in the external data set, the resulting AUC was 0.71.

The final model for the prediction of vitamin D concentrations <30 nmol/L consisted of 10 predictors: older age, smoking, alcohol consumption (<13 drinks/wk), season, no vitamin supplement use, no bicycling, no gardening, medication use, limitations in the use of own or public transportation, and the inability to remember the present year. After internal validation, the resulting AUC was 0.80 and Nagelkerke’s \( R^2 \) was 0.28. The probability of vitamin D deficiency for a 65-y-old individual ranged from 0.2% to 45% according to the number of predictors. For an 80-y-old individual, these respective probabilities were 0.8% to 72%. The Hosmer-Lemeshow goodness-of-fit test was not significant in the majority of the imputed data sets. External validation in our validation sample was not possible; only 3.8% of the participants had vitamin D concentrations <30 nmol/L.

All regression coefficients were transformed into simple scores (see Table 2) to enable general practitioners or other health care professionals to easily use the models and to predict the risk of being vitamin D deficient. The total score of the model for <50 nmol/L ranged from 8 to 97, whereas the scores ranged from 6 to 204 for the <30-nmol/L model. The probability of having a serum 25(OH)D concentration <50 nmol/L per each 10-point increase in the total risk score and the prevalence of these scores in our sample are shown in Figure 1. A participant with a score between 71 and 80 has an 87% chance of being vitamin D deficient (<50 nmol/L), whereas a person with a score between 11 and 20 has a 3% chance.

The diagnostic and predictive values of both developed models, according to different cutoffs (per 10 or 20 points) in the total risk score, are shown in Tables 3 and 4. In both models, the lower the cutoff, the lower the sensitivity and the higher the specificity. The higher the cutoff, the higher the specificity and the lower the sensitivity.

**DISCUSSION**

This study showed that serum 25(OH)D concentrations <50 and <30 nmol/L could be predicted accurately by easily assessable predictors. We identified older age, sex (female), higher BMI, smoking, less alcohol use, season, no vitamin supplement use, no bicycling, no sporting, no gardening, medication use, poor appetite, and having no partner as predictors for concentrations <50 nmol/L. For vitamin D concentrations <30 nmol/L, older age, smoking, less alcohol use, season, no vitamin supplement use, no bicycling, no gardening, medication use, limitations in the use of transportation, and the inability to remember the present year were identified as the final predictors.
To the best of our knowledge, our study is the first that successfully developed models to predict vitamin D deficiency in the general older European population. Most previous studies describe a prediction model for concentrations of serum 25(OH)D instead of vitamin D deficiency (27–30). The explained variance of serum 25(OH)D in these models ranged from 21% to 40% (27–30). In our models, Nagelkerke’s $R^2$ were 0.31 and 0.28, which could be interpreted as pseudo-explained variance. In general, for logistic regression models, these values are lower and must be interpreted carefully; Nagelkerke’s $R^2$ is not the same as explained variance based on linear models (31). AUCs were 0.78 and 0.80 for our models, which means that 78% and 80% of the participants, respectively, were classified correctly. After external validation of the <50-nmol/L model, the AUC was still 0.71. Three previous studies performed analyses on the prediction of vitamin D deficiency in non-European populations (14, 32, 33). However, one study did not report the AUC at all (33); the second reported AUCs of 0.79–0.80 for different models with different cutoffs for vitamin D deficiency and, after external validation, these remained at 0.65–0.70 (32). The performance of the latter models is comparable to ours, but the contents of the models are different. In our model, only easily assessable predictors were included. In the previous models, laboratory variables, such as serum calcium, albumin, or parathyroid hormone, were also included. By including these variables, there will be a restriction in cost savings. In addition, these analyses were performed in dialysis patients and not in the general older population (32). The third and most recent study was performed in Australia (14). The performance of these reported models was comparable to ours, but the predictors included in the model are also more challenging to assess. For example, physical activity was measured in metabolic equivalent task hours/wk (an indicator for energy expenditure during activities). In our model, this was assessed by a simple question including physical activity was measured in metabolic equivalent task hours/wk (an indicator for energy expenditure during activities). In our model, this was assessed by a simple question...
on whether a participant cycles or walks outdoors (yes or no). Another difference is that season was not included in the models because in Australia this may be of less influence on vitamin D status compared with The Netherlands. Season was one of the strongest predictors in our models. This means that the same individual will have a higher total score in the winter than in the summer or spring. With a higher total score, the probability of being vitamin D deficient or insufficient will be higher, which means that it may depend on the season whether an individual needs vitamin D supplements.

Our results may have practical implications with respect to identifying persons at risk of low vitamin D status, and thereby may influence the need for vitamin D supplementation or measurement of serum 25(OH)D concentration. At present, the Dutch guidelines for supplementing vitamin D are quite general (9). By using our model, the risk could be calculated and vitamin D supplement use (or serum vitamin D testing) may be more specifically advised on the basis of the prediction of a low serum 25(OH)D. This will contribute to health care cost savings.

The developed models may be used in several ways. First, they can be used to identify individuals at such a high risk of low vitamin D status that vitamin D supplements can be recommended without further testing of serum 25(OH)D. Second, the risk models can be used to identify persons in whom low vitamin D status is very unlikely and who therefore may not require vitamin D supplementation. For individuals with an intermediate risk, serum 25(OH)D determination is required to make a definite decision on whether vitamin D supplements are needed or whether these individuals can simply be advised to take vitamin D supplements. This latter decision will depend on the preferences of the patient and physician. To determine the ideal cutoffs for the 2 mentioned aims, Table 3 can be used. For the first aim, ie, to predict individuals at high risk of vitamin D deficiency (<50 nmol/L), the cutoff in the total risk score may be 68. By choosing this cutoff, 21.1% will be classified as deficient.

### TABLE 2

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Regression coefficient (B), after internal validation</th>
<th>OR (95% CI)</th>
<th>Score</th>
<th>Regression coefficient (B), after internal validation</th>
<th>OR (95% CI)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-3.899</td>
<td></td>
<td></td>
<td>-6.032</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.071</td>
<td>1.1 (1.1, 1.1)</td>
<td>1 (per year &gt;65 y)</td>
<td>0.077</td>
<td>1.1 (1.1, 1.1)</td>
<td>2 (per year &gt;65 y)</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.441</td>
<td>1.6 (1.1, 2.2)</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m²) &gt;30</td>
<td>0.261</td>
<td>1.3 (0.9, 1.8)</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Smoking: yes</td>
<td>0.345</td>
<td>1.6 (1.1, 2.2)</td>
<td>5</td>
<td>0.494</td>
<td>1.7 (1.1, 2.5)</td>
<td>13</td>
</tr>
<tr>
<td>Alcohol use: &lt;13 drinks/wk</td>
<td>0.400</td>
<td>1.6 (1.1, 2.3)</td>
<td>6</td>
<td>1.037</td>
<td>3.0 (1.8, 5.0)</td>
<td>28</td>
</tr>
<tr>
<td>Season</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Winter</td>
<td>0.820</td>
<td>2.2 (1.5, 3.3)</td>
<td>12</td>
<td>0.761</td>
<td>2.2 (1.4, 3.5)</td>
<td>21</td>
</tr>
<tr>
<td>Spring</td>
<td>1.092</td>
<td>3.1 (2.1, 4.7)</td>
<td>15</td>
<td>0.471</td>
<td>1.6 (1.0, 2.7)</td>
<td>13</td>
</tr>
<tr>
<td>Summer</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Autumn</td>
<td>0.201</td>
<td>1.1 (0.8, 1.7)</td>
<td>3</td>
<td>0.037</td>
<td>1.0 (0.6, 1.7)</td>
<td>1</td>
</tr>
<tr>
<td>Vitamin use: no</td>
<td>0.616</td>
<td>1.8 (1.3, 2.5)</td>
<td>9</td>
<td>0.729</td>
<td>2.2 (1.4, 3.3)</td>
<td>20</td>
</tr>
<tr>
<td>Bicycling: no</td>
<td>0.583</td>
<td>1.8 (1.3, 2.4)</td>
<td>8</td>
<td>0.728</td>
<td>2.1 (1.5, 3.2)</td>
<td>20</td>
</tr>
<tr>
<td>Sporting: no</td>
<td>0.387</td>
<td>1.5 (1.1, 2.0)</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gardening: no</td>
<td>0.541</td>
<td>1.7 (1.3, 2.3)</td>
<td>8</td>
<td>0.787</td>
<td>2.3 (1.5, 3.5)</td>
<td>21</td>
</tr>
<tr>
<td>Medication use: yes</td>
<td>0.272</td>
<td>1.3 (1.0, 1.8)</td>
<td>4</td>
<td>0.324</td>
<td>1.4 (0.9, 2.2)</td>
<td>9</td>
</tr>
<tr>
<td>Presence of appetite: no</td>
<td>0.305</td>
<td>1.5 (1.0, 2.3)</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Limitations in transport use: yes</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.425</td>
<td>1.6 (1.1, 2.3)</td>
<td>12</td>
</tr>
<tr>
<td>Partner status: no partner</td>
<td>0.380</td>
<td>1.4 (1.0, 1.9)</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Remembers year: no</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.546</td>
<td>1.8 (0.9, 3.4)</td>
<td>15</td>
</tr>
</tbody>
</table>

1 ORs were calculated by using multiple logistic regression analysis. n = 1509 for both models. 25(OH)D, 25-hydroxyvitamin D.

2 The score is the regression coefficient divided by the lowest regression coefficient, which is the coefficient of age for <50 nmol/L and of summer for <30 nmol/L and rounded to the nearest integer. A higher score indicates a higher risk of vitamin D deficiency.
Eighty-six percent of individuals classified as deficient according to the model are actually deficient (positive predictive value). This means that only 14% of those with a positive score will be wrongly advised to take vitamin D supplements (44 of the 1509 participants). For the second aim, ie, to identify individuals in whom low vitamin D status is unlikely, the cutoff may be 38 points. By choosing this cutoff, 20.4% of the individuals will be classified as sufficient; 84.1% of participants who are classified as sufficient will actually have a more than sufficient vitamin D status, meaning that only 15.9% of these individuals classified as “sufficient” will not be advised to take vitamin D supplements when they actually should be taking them (49 of the 1509 participants). The same procedure to define cutoffs can be used within the other model. However, in the future, further discussion on the optimal cutoffs of the total risk score for high and low risk is necessary.

Although the prediction model for concentrations <50 nmol/L in this study was successfully validated in an external population, it should be noted that it cannot be automatically used in every population. This study was performed in a relatively healthy older population and the external validation data set was based on a comparable population type. Whether the risk score can be used in, for example, institutionalized and frail older people still needs to be determined.

In addition to the mentioned uncertainty on the generalizability of this model to other populations, this study has some limitations. The LASA does not have detailed information on the use of vitamin D supplements. Therefore, we used the use of over-the-counter multivitamin supplements in our model, but this may not necessarily reflect the use of vitamin D supplements. Last, the validation sample consisted of somewhat younger individuals than the participants in the development sample and the measurements took place >13 y later. Therefore, the performance of the model in the external data set may be underestimated. The strengths of this study are the large sample sizes and the method of recruitment of the participants, which reflects the Dutch older population in general. Furthermore, by using a multiple imputation technique, no participants were excluded from the analysis because of one or more missing values.

### TABLE 3

Dissociative values of the developed risk profile for serum 25(OH)D <30 nmol/L at different cutoffs in the total risk score

<table>
<thead>
<tr>
<th>Cutoff in the total risk score</th>
<th>Group</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PV+</th>
<th>PV–</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤8</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
<td>100.1</td>
<td>18.5</td>
</tr>
<tr>
<td>≤18</td>
<td>98.5%</td>
<td>99.7%</td>
<td>2.8%</td>
<td>102.5</td>
<td>51.1</td>
</tr>
<tr>
<td>≤28</td>
<td>93.0%</td>
<td>98.7%</td>
<td>12.7%</td>
<td>111.4</td>
<td>53.6</td>
</tr>
<tr>
<td>≤38</td>
<td>79.6%</td>
<td>93.6%</td>
<td>34.7%</td>
<td>128.3</td>
<td>59.4</td>
</tr>
<tr>
<td>≤48</td>
<td>59.5%</td>
<td>79.5%</td>
<td>60.9%</td>
<td>140.4</td>
<td>67.5</td>
</tr>
<tr>
<td>≤58</td>
<td>39.5%</td>
<td>60.0%</td>
<td>82.1%</td>
<td>142.7</td>
<td>77.5</td>
</tr>
<tr>
<td>≤68</td>
<td>21.1%</td>
<td>36.1%</td>
<td>94.1%</td>
<td>130.2</td>
<td>86.2</td>
</tr>
<tr>
<td>≤78</td>
<td>7.4%</td>
<td>12.9%</td>
<td>98.3%</td>
<td>111.2</td>
<td>88.3</td>
</tr>
<tr>
<td>≤88</td>
<td>1.3%</td>
<td>25.9%</td>
<td>99.9%</td>
<td>102.4</td>
<td>95.0</td>
</tr>
</tbody>
</table>

1. Scores higher than the cutoff scores indicate that vitamin D deficiency is present according to the risk model. n = 1509. PV+, positive predictive value; PV–, negative predictive value; Σ, sum of sensitivity and specificity; 25(OH)D, 25-hydroxyvitamin D.

### REFERENCES


