PART III

Relationship of serum 25(OH)D with quality of life and effects in COPD
CHAPTER 6
Associations of serum 25-hydroxyvitamin D concentrations with quality of life and self-rated health in an older population

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Abstract

Context
Vitamin D deficiency has been associated with impaired physical functioning, depression and several chronic diseases and might thereby affect quality of life and self-rated health.

Objective
The aim of this study was to assess relationships of serum 25-hydroxyvitamin D (25(OH)D) with quality of life and self-rated health, and to examine whether physical performance, depressive symptoms and number of chronic diseases mediate these relationships.

Design
We analysed data from the Longitudinal Aging Study Amsterdam, an ongoing population-based cohort study of older Dutch individuals.

Main outcome measures
Serum 25(OH)D was classified into categories: <25, 25-50 and ≥50 nmol/L. We assessed quality of life (QoL) using the SF-12 Health Survey (n=862) and self-rated health (SRH) with a single question, dichotomized into good versus poor SRH (n=1248).

Results
Individuals with serum 25(OH)D <25 nmol/L scored lower on the physical component score of the SF-12 and had a lower odds on good SRH score compared to individuals with serum 25(OH)D ≥50 nmol/l (Beta(95%CI): -3.9(-6.5 to -1.3) for SF-12, and odds ratio(95%CI): 0.50(0.33 to 0.76) for SRH). Physical performance, depressive symptoms and number of chronic diseases were associated with vitamin D status, QoL and SRH. Adding all these potential mediators to regression models attenuated associations of 25(OH)D <25 nmol/L with QoL with 78% and SRH with 32%.

Conclusion
Lower 25(OH)D status is related to lower scores on QoL and SRH. Large part of the association with QoL can statistically be explained by physical performance, depressive symptoms and number of chronic diseases.
Introduction

Vitamin D has a broad effect on health. Vitamin D deficiency may cause bone mineralization defects which may lead to osteoporosis and fractures (1). Also, it has been shown to be associated with multiple chronic diseases such as cardiovascular diseases, diabetes, cancer and auto-immune diseases (2). Vitamin D contributes to optimal physical functioning and muscle strength (3;4). In addition, low vitamin D status has been related to depressive disorders (5). Epidemiologic studies showed that vitamin D deficiency is highly prevalent, especially in older individuals and patients with chronic diseases, with a prevalence ranging from 40 to 100% (2;6). Vitamin D status might also be associated with quality of life and self-rated health, although studies on these latter relationships are scarce.

Quality of life is the subjective evaluation of one's own physical, mental and social functioning. It is determined by many factors and can be arranged according to several dimensions. Quality of life is an important outcome in epidemiologic studies, randomized controlled trials (RCT’s) and cost-utility studies. A related parameter to quality of life is self-rated health. Self-rated health is the perception of one's own health and a summary measure of health status. Self-rated health gives a good indication of one’s health and has proven to be a predictor of mortality (7;8). Relationships between vitamin D status and quality of life and self-rated health may be mediated by several factors. Patients with chronic diseases and persons with mobility limitations score lower in questionnaires on quality of life (9;10). Self-rated health is correlated with number of chronic diseases and might therefore be associated with vitamin D status (11). Depression is an important predictor of quality of life and self-rated health and might also mediate the relationship with vitamin D status (12).

In this study we aimed to assess relationships between serum 25(OH)D-concentrations and quality of life and self-rated health in a population-based cohort of older Dutch individuals. In addition, we examined the role of physical performance, number of chronic diseases and depressive symptoms as potential mediators.

Methods

Study participants

The Longitudinal Ageing Study Amsterdam (LASA) is a population-based cohort study on predictors and consequences of healthy aging in an older Dutch population. The outline of the study has been described elsewhere (13;14). For the current study data from the second (1995/1996) and third cycle (1998/1999) were used. In 1995/1996 medical data were obtained from 1509 participants who were aged 65 years and older as of January 1,
1996. Participants underwent a medical interview including the question on self-rated health. Participants without a blood sample, with incomplete or no performance tests or with missing values for potential confounders were excluded. This resulted in data of 1248 participants in the statistical analysis. Data on quality of life were collected in 1998/1999, during the third cycle. QoL-questionnaires were completed by 862 of 1248 participants. The study was approved by the Medical Ethics Committee of the VU University Medical Center, and informed consent was obtained from all participants.

**Serum 25-OH vitamin D**

In 1995–1996, fasting morning blood samples were collected and centrifuged. Serum samples were stored at -20 °C, and serum 25-hydroxyvitamin D (25(OH)D) was measured by a competitive protein-binding assay (Nichols Diagnostics, San Juan Capistrano, CA) in 1997/1998 at the Endocrine Laboratory of the VU University Medical Center. The interassay coefficient of variation was 10%.

**SF-12**

The SF-12 Health Survey is a multidimensional short-form (SF) generic measure of health status. It is a valid subset of the larger SF-36 and monitors health in general and specific populations. Two subscales are derived from the SF-12: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). These summary scales based on the SF-12 correlate very highly with the SF-36 version (15). Each of the subscales is scored within the 0 to 100 range with a higher score indicating better health-related quality of life. Data are obtained by a self-administered questionnaire during the third measurement-cycle in 1998/1999.

**Self-rated health**

Self-rated health is evaluated by asking the participants how they perceive their health in general. There are five response categories: 1) 'poor', 2) 'sometimes good/bad', 3) 'fair', 4) 'good' and (5) 'excellent' (16). Data were obtained during the second cycle in 1995/1996.

**Mediators: number of chronic diseases, physical performance and depressive symptoms**

The selection of seven major chronic diseases was based on their prevalence (>5%) in the 55+ age group in The Netherlands (17). These were: chronic obstructive pulmonary disease (asthma, chronic bronchitis and pulmonary emphysema), cardiac disease, peripheral arterial disease, stroke, diabetes mellitus, rheumatoid arthritis/osteoarthritis and cancer. Information about the diseases was based on self-report (18). Physical performance was assessed by means of three performance tests. The scores were
serum to obtain a total performance score (4;19). The tests included: the time taken to
walk 3 m, turn 180° and walk back as fast as possible (walking test); time needed to rise
times from a chair with arms folded in front of the chest (chair stands test); and the
ability to stand with the heel of one foot directly in front of, and touching the toes of the
other foot for at least 10 sec (tandem stand). For the walking test and the chair stands test
one to four points could be scored corresponding to the quartile of the distribution of time
needed. Score 0 was given to those respondents who could not complete a test. The score
of the tandem test was categorized into three groups: unable (0 points), able to hold position
for 3-9 seconds (2 points), and able to hold position for 10 seconds (4 points). Total score
ranged from 0 to 12, with 12 points representing an excellent performance (20).
Depressive symptoms were measured using a self-report rating scale (CES-D) (21;22). The
total score on the CES-D ranges between 0 and 60. To identify those with clinically relevant
levels of symptoms, a cutoff score of 16 or more is generally used (23). Data were gathered
in face-to-face interviews.
Data of the second measurement cycle in 1995/1996 were used for all potential mediators

Confounders
The following potential confounders, measured in 1995/1996, were included in the statistical
analysis: gender, age, body mass index (BMI), alcohol consumption, smoking status, season
of blood collection and serum creatinine. Body weight was measured without clothes and
shoes, using a calibrated balance beam scale. Body height was measured with a stadiometer.
The alcohol consumption index was used to classify alcohol drinkers into four categories
(non-drinker, light drinkers, moderate drinker and (very) excessive drinker) based on the
number of days on which alcohol was consumed and the number of alcoholic drinks
consumed each time (24). Information on smoking status was based on self-report and was
classified as never smoked, former smoker, or current smoker. Season for blood collection
was dichotomized in winter (October–March) and summer (April–September). Vitamin
D synthesis depends on sun exposure and season, and in The Netherlands it is not
synthesized between October and March (25). Serum creatinine was used as a marker of
renal function and was analysed according to standard laboratory methods.

Statistical analysis
To assess differences in baseline characteristics between 25(OH)D categories, Pearson χ²
tests was used for categorical variables, ANOVA for normally distributed continuous
variables and the Kruskall-Wallis H test for skewed continuous variables.
Multiple linear regression analysis was used to investigate the association between serum
25(OH)D and SF-12 scores. Because the relationship between serum 25(OH)D and SF-12
scores was not linear, vitamin D was categorized into three categories using traditional
cut-off points (1): <25 nmol/L, 25-50 nmol/L, ≥50 nmol/L. The vitamin D category of ≥50 nmol/L served as reference category. SF-12 scores were used as a continuous variable. For the association of serum 25(OH)D and self-rated health a logistic regression analysis was used. Self-rated health (SRH) scores were dichotomized into ‘good self-rated health’ and ‘poor self-rated health’. The first category (good SRH) included the scores ‘excellent’ and ‘good’ and the second category (poor SRH) contained the scores ‘fair’, ‘sometimes good/bad’ and ‘poor’ (16). In the analyses we compared the odds for each vitamin D category to respond with ‘good SRH’ versus ‘poor SRH’. Again, vitamin D category of ≥50 nmol/L served as a reference category.

We used restricted cubic spline plots to estimate an optimal cut-off level for serum 25(OH)D in the relationship with SF-12 scores. Cubic splines are piecewise polynomial functions that are constrained to join smoothly at points called knots. These spline functions provide better insight into dose-response relationships compared with analyses using categorized variables. Restricted cubic spline functions use all data points to estimate the risk at each level of exposure, as opposed to step functions using categorical variables, which assume a constant risk within categories. Cubic spline functions were tested in regression models at three knots using spline plots and likelihood ratio tests. All spline regression analyses were performed using R version 2.15.0.

To assess whether physical performance, number of chronic diseases and depressive symptoms acted as mediators, a statistical mediator analysis was performed according to Baron and Kenney (26) (Figure 1). A mediator is a variable that specifies how a given effect occurs. According to the model of Baron and Kenney, a variable can be considered a mediator if four conditions are met: 1) the predictor (A) must be significantly associated with the hypothesized mediator (B), 2) the predictor (A) must be significantly associated with the hypothesized measure (C), 3) the mediator (B) must be significantly associated with the dependent variable (C) and 4) the impact of the predictor (A) on the dependent variable (C) is less after controlling for the mediator (B). In our models we first analysed associations of vitamin D status (predictor) with quality of life and self-rated health (dependent variables). Then, we studied associations of vitamin D status (predictor) with physical performance, number of chronic diseases and depressive symptoms (mediators). Subsequently, relationships between physical performance, number of chronic diseases and depressive symptoms (mediators) with SF-12 scores and self-rated health (dependent variables) were analysed. Finally, physical performance, number of chronic diseases and depressive symptoms (mediators) were added separately and together to the regression models to examine the contribution of these potential mediators to the association between vitamin D category (predictor) and both quality of life and self-rated health (dependent variables).
Results

Participants included in the analyses (n=1248) were younger than the total study population (n=1509, mean age(SD): 75.6(6.6) versus 78.5(6.6), P<0.001) and had an identical gender distribution. Participants who completed the QoL-questionnaire were younger (74.1(6.0) versus 78.5(6.6), P<0.001) than the total study population in 1998/1999 (n=1509).

Characteristics of participants are shown in Table 1 stratified to serum 25(OH)D category. Participants in the lower categories, as compared to the highest category of 25(OH)D concentrations, were older and more often female. They had lower scores on physical performance tests, more chronic diseases and more depressive symptoms. Participants from the lowest vitamin D category scored lower on the physical component of the SF-12 and on self-rated health as compared to the highest category. The mental component score of the SF-12 did not vary between the categories of serum 25(OH)D.

The findings of the regression models are shown in Table 2. The first model (model A) showed an association of serum 25(OH)D with the physical component score of the SF-12 after adjustment for confounders. The score in the lowest category of serum 25(OH)D was 3.9 points lower (CI -6.5 to -1.3) than in the reference category. Figure 2 shows the multivariable spline function of serum 25(OH)D and the physical component score of the SF-12. Up to serum 25(OH)D levels of approximately 70 nmol/L, the SF-12 score increased with increasing serum 25(OH)D. Serum 25(OH)D was not associated with scores of the mental component of the SF-12 (data not shown).

Serum 25(OH)D was significantly associated with scores on self-rated health. Participants from the lowest category of 25(OH)D had lower odds to score higher on self-rated health compared to participants from the highest category of serum 25(OH)D (Table 2, model A).

To investigate whether physical performance and number of chronic diseases acted as mediators, a mediator analysis according to Baron and Kenney was performed (Figure 1, Table 3). Participants from the lowest category of serum 25(OH)D scored lower on physical
Performance, had more chronic diseases and more depressive symptoms compared to participants from the highest category (condition 1). As we stated earlier, a significant association of vitamin D status and SF-12 and SRH scores was shown in Table 2 (condition 2). Physical performance, number of chronic diseases and depressive symptoms were related to SF-12 scores and self-rated health (Table 3). Participants with a better score on physical performance, less chronic diseases and less depressive symptoms scored higher on SF-12 and had higher odds on good self-rated health (condition 3). The last step in the analysis

| Table 1. Baseline characteristics of the study population according to 25(OH)D-categories. |
|---------------------------------------|---------------------------------|---------------------------------|
| 25(OH) vitamin D (nmol/L)             | Overall P                        |
|---------------------------------------|---------------------------------|---------------------------------|
|                                       | < 25 (n=135)                    | 25 - 50 (n=460)                 | > 50 (n=653)                    |
| Age in years                          | 79.9 (5.9)                      | 77.0 (6.6)                      | 73.4 (5.8)                      |
| Gender                                | <0.001                          | <0.001                          | 0.003                           |
| Women                                 | 63.0                             | 59.8                            | 42.6                            |
| BMI (kg/m²)                           | 27.4 (5.3)                      | 27.3 (4.4)                      | 26.5 (3.7)                      |
| Creatinine (µmol/L)                   | 91.8 (35.8)                     | 97.2 (50.1)                     | 94.7 (20.5)                     |
| Smoking                               | <0.001                          | <0.001                          | 0.003                           |
| Never smoker                          | 48.9                             | 38.9                            | 30.3                            |
| Former smoker                         | 28.1                             | 42.0                            | 52.8                            |
| Current smoker                        | 23.0                             | 19.1                            | 16.8                            |
| Alcohol use                           | <0.001                          | <0.001                          | 0.003                           |
| None                                  | 31.1                             | 30.4                            | 17.6                            |
| Light                                 | 53.3                             | 48.7                            | 51.0                            |
| Moderate                              | 14.8                             | 15.0                            | 24.0                            |
| (Very) excessive                      | 0.7                              | 5.9                             | 7.4                             |
| Season of blood collection            | <0.001                          | <0.001                          | 0.003                           |
| Winter                                | 68.1                             | 57.2                            | 49.2                            |
| Physical performance score            | 5.0 (3.1)                       | 6.8 (3.2)                       | 8.3 (2.7)                       |
| Number of chronic diseases            | 1.0 (1.0-2.0)                   | 1.0 (0.0-2.0)                   | 1.0 (0.0-2.0)                   |
| CES-D score                           | 9.9 (9.2)                       | 8.8 (7.8)                       | 6.6 (7.0)                       |
| SF-12 score                           | 38.4 (11.9)                     | 43.2 (11.2)                     | 46.0 (9.7)                      |
| Self-rated health score               | <0.001                          | <0.001                          | 0.003                           |
| Poor                                  | 6.0                              | 2.4                             | 2.6                             |
| Sometimes good/bad                    | 13.4                             | 11.8                            | 7.9                             |
| Fair                                  | 34.2                             | 25.9                            | 21.9                            |
| Good                                  | 39.6                             | 49.6                            | 54.9                            |
| Excellent                             | 6.7                              | 10.2                            | 12.6                            |

Data are presented as mean (s.d.), percentages or median (interquartile range).
is the adjustment for the potential mediators. In Table 2, the regression models are shown after adjusting for number of chronic diseases (model B), depressive symptoms (model C) and physical performance (model D) (condition 4). Adjustment for number of chronic diseases decreased the strength of the association of 25(OH)D with the physical component of SF-12 and self-rated health with 33% and 8%, respectively. Adjustment for depressive symptoms decreased the strength of the associations with 26% and 20% respectively. Adjustment for physical performance decreased the strength of the associations with 54% and 24%, respectively. Adding the three mediators together to the models decreased the strength of the association with quality of life with 78% and the strength of the association with self-rated health with 32% (Model E).

Discussion

This is the first population-based study that shows an association between serum 25(OH)D concentrations and quality of life and self-rated health in an older population. Participants with lower cross-sectional serum concentrations scored lower on the physical component of the SF-12 and self-rated health. Physical performance, number of chronic diseases and depressive symptoms acted as mediators and largely explained the relationship between vitamin D and quality of life.
### Table 2. Results of regression analyses of serum 25(OH)D with SF-12 scores and self-rated health scores

<table>
<thead>
<tr>
<th>25(OH)D (nmol/L)</th>
<th>A¹</th>
<th>B²</th>
<th>C³</th>
<th>D⁴</th>
<th>E⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SF-12 physical component (n=862)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 B (95%CI)</td>
<td>-3.9 (-6.5 to -1.3)</td>
<td>-2.6 (-5.1 to -0.2)</td>
<td>-2.9 (-5.4 to -0.3)</td>
<td>-1.8 (-4.3 to 0.6)</td>
<td>-0.9 (-3.2 to 1.5)</td>
</tr>
<tr>
<td>P</td>
<td>0.004</td>
<td>0.035</td>
<td>0.029</td>
<td>0.147</td>
<td>0.466</td>
</tr>
<tr>
<td>25–50 B (95%CI)</td>
<td>-0.8 (-2.3 to 0.6)</td>
<td>-0.6 (-2.0 to 0.8)</td>
<td>-0.5 (-2.0 to 0.9)</td>
<td>-0.0 (-1.4 to 1.4)</td>
<td>0.1 (-1.2 to 1.4)</td>
</tr>
<tr>
<td>P</td>
<td>0.264</td>
<td>0.389</td>
<td>0.468</td>
<td>0.968</td>
<td>0.857</td>
</tr>
<tr>
<td>&gt;50 Reference category</td>
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| Self-rated health cross-sectional (n=1248)* | | | | | |
| <25 OR (95%CI) | 0.50 (0.33 to 0.76) | 0.55 (0.35 to 0.85) | 0.62 (0.40 to 0.94) | 0.66 (0.42 to 1.02) | 0.73 (0.45 to 1.18) |
| P | 0.001 | 0.008 | 0.025 | 0.060 | 0.192 |
| 25–50 OR (95%CI) | 0.88 (0.67 to 1.15) | 0.91 (0.68 to 1.22) | 0.97 (0.73 to 1.29) | 0.96 (0.72 to 1.27) | 1.03 (0.76 to 1.41) |
| P | 0.355 | 0.538 | 0.879 | 0.796 | 0.842 |
| >50 Reference category | | | | | |

B: regression coefficient B derived from linear regression analyses; OR: Odds ratio derived from logistic regression analyses.

1. Model A: adjustments were made for gender, age, BMI, alcohol consumption, smoking status, season of blood collection and serum creatinine.
2. Model B: as model A with adjustment for number of chronic diseases.
3. Model C: as model A with adjustment for depressive symptoms (CES-D score).
4. Model D: as model A with adjustment for physical performance.
5. Model E: as model A with adjustment for number of chronic diseases, depressive symptoms and physical performance.

* Good versus poor SRH: odds for good SRH
This outcome is in line with other observational studies that have been performed in other populations. These studies showed that low serum 25(OH)D was associated with impaired quality of life. In patients with Crohn's disease, vitamin D deficiency was independently associated with lower scores on questionnaires on quality of life (27). In a study in dialysis patients, vitamin D deficiency was also associated with poorer quality of life (28). In that study, vitamin D status was associated with the mental component of the SF-12 and not with the physical component. The difference between the latter and our study might be explained by the difference in study populations, dialysis patients versus a population-based cohort of older individuals. The prevalence of vitamin D deficiency in the study with dialysis patients (65%) was higher than in our study (48%). Dialysis therapy has a great impact on social functioning and dependency and might therefore influence the mental aspect of quality of life more than the physical aspect. In a study among Turkish women with osteoporosis, lower serum 25(OH)D was associated with impaired quality of life (QoL), both for patients with and without fractures (29). In this study no correlation was found between vitamin D status and number of concomitant diseases. In our study we found a significant association between vitamin D categories and number of chronic diseases. Participants in the lowest 25(OH)D category had 0.2 chronic diseases more compared to participants in the highest category. This difference might be explained by the exclusion criteria used in the study with women with osteoporosis. In that study persons with diseases affecting quality of life (e.g. cancer, chronic renal insufficiencies, chronic respiratory diseases, decompensate cardiovascular diseases and fracture within the 6 months of the study) were excluded. This influences the number of concomitant diseases and might therefore alter associations with serum 25(OH)D.

To assess whether vitamin D is a cause or a consequence of low quality of life, the effect of vitamin D supplementation on quality of life should be investigated. In a RCT among community dwelling older women at increased risk of a hip fracture, vitamin D supplementation did not improve quality of life after 6 and 12 months follow-up (30). In another RCT, vitamin D supplementation during 20 weeks in vitamin D deficient (<50 nmol/L) older patients with heart failure did not improve quality of life (31). In a RCT among elderly people with a low-trauma fracture in the past years vitamin D supplementation during 2 years did not improve quality of life (32). The lack of an effect of vitamin D supplementation in these studies suggests that vitamin D is an indicator rather than a cause of impaired quality of life. However, in two of the above three studies vitamin D status was not assessed and participants might not have been deficient enough to show a beneficial effect of vitamin D supplementation. This suggestion is in line with our findings. Vitamin D deficiency (25(OH)D<25 nmol/l) but not vitamin D insufficiency (25(OH)D 25-50 nmol/l) was associated with a decrease in quality of life.
Our study showed that vitamin D status was associated with self-rated health. To the best of our knowledge, this is the first study that investigated the association between serum 25(OH)D and self-rated health. Other studies used self-rated health as a part of QoL-scores, but did not analyse the association between vitamin D status and self-rated health as such. This study also showed that large part of the association of vitamin D status with the physical component of quality of life and self-rated health can be statistically explained by physical performance. These findings are in line with several studies, which have shown a positive association of vitamin D with physical performance and muscle strength (3;4). Several RCTs also showed a positive effect of vitamin D supplementation on muscular function (33;34). An impaired physical function may lead to a lower quality of life because of loss of autonomy and impaired social functioning.

Number of chronic diseases was also a statistical mediator of the relationship between vitamin D and the physical component of quality of life and for a smaller part of the association with self-rated health. A possible explanation for the small mediating effect on the relationship between vitamin D and self-rated health might be the frame of reference of persons with several chronic diseases. Persons with chronic diseases may adapt their health perceptions to the presence of their diseases (response shift). An epidemiologic study investigating the 17-year time trend of self-rated health showed a stable trend in self-rated health, while the mean number of chronic diseases and the prevalence of mild disability increased (35). The results of this study indicated that a shift took place in which factors were deemed important for self-rated health. People focused more on poor functioning, but less on their diseases. In addition, when rating their health, people often implicitly applied social comparison.

Depressive symptoms also mediated the relationship between vitamin D status and the physical component of quality of life and self-rated health. Several studies have investigated the relationship between vitamin D status and depression and results are conflicting (5;36;37). On the one hand vitamin D deficiency might be a consequence of depression, as underlying causes of vitamin D deficiency such as decreased outdoor activity are secondary to depression. On the other hand vitamin D has been proved to influence several mediators, which are believed to play a role in the pathogenesis of depression (38;39). Vitamin D deficiency can also cause hyperparathyroidism which is often associated with mood disorders, which disappear after normalising PTH levels (40).

The three mediators together explain 78% of the association between vitamin D status and quality of life and 32% of the association between vitamin D status and self-rated health. Physical performance explains the largest part of these associations. A part of the associations remains unexplained. This might be due to inaccuracy of the measurement instruments. The remaining part of the associations might also be mediated by other unknown variables. Associations with self-rated health remain largely unexplained which
implies other contributing variables to play a role which remains to be examined in further studies.

The strengths of the present study are its large study population and population-based nature. Outcomes of this study can be applied to the general older population. A limitation is the fact that SF-12 was not measured at baseline but after three years. Despite this, we did find an association between vitamin D status and SF12-scores. Another limitation is the potential selection bias that occurred in the population that filled in the SF12-questionnaire. These participants were younger than the total study population. This may have led to an underestimation of the association. In addition, number of chronic diseases was not objectively assessed but by self-report of respondents.

In conclusion, results of this population-based study show that lower serum 25(OH)D is associated with lower scores on quality of life and self-rated health. Large part of this association can statistically be explained by physical performance, number of chronic diseases and depressive symptoms. A part of the association of vitamin D status and self-rated health remains unexplained by these mediators. It is important to further investigate these associations, because of the high prevalence of vitamin D deficiency and the great impact of impaired quality of life. In addition, treatment of vitamin D deficiency is easy and safe. To investigate whether vitamin D deficiency is a cause or just an indicator of low quality of life, additional randomized controlled trials in vitamin D deficient individuals are essential.
References


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