25. Morello A, Lloyd-Jones DM, Chae CU *et al*. Association of atrial fibrillation and amino-terminal pro-brain natriuretic peptide concentrations in dyspneic subjects with and without acute heart failure: results from the ProBNP Investigation of Dyspnea in the Emergency Department (PRIDE) study. Am Heart J 2007; 153: 90–7.
26. van Bemmel T, Gussekloo J, Westendorp RG, Blauw GJ. In a population-based prospective study, no association between high blood pressure and mortality after age 85 years. J Hypertens 2006; 24: 287–92.
27. Oates DJ, Berlowitz DR, Glickman ME, Silliman RA, Borzecki AM. Blood pressure and survival in the oldest old. J Am Geriatr Soc 2007; 55: 383–8.
28. Weverling-Rijnsburger AW, Blauw GJ, Lagaay AM *et al*. Total cholesterol and risk of mortality in the oldest old. Lancet 1997; 350: 1119–23.

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Determinants of 25-hydroxyvitamin D in older Irish adults

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Abstract

Background: vitamin D deficiency is prevalent in older adults living in Northern Europe and is influenced by several factors which may vary significantly with age.
Objective: we aimed to investigate the determinants of 25-hydroxyvitamin D [25(OH)D] in older Irish adults and in particular to examine the effect of supplement use and surrogate markers of sun exposure.
Methods: subjects were non-institutionalised community dwelling Irish adults aged over 60 years who were participants of a large cross-sectional study comprising three disease defined cohorts. Serum 25(OH)D was measured by liquid chromatography mass spectroscopy. Associations between 25(OH)D and potential confounders were explored in forward regression models in each cohort.
Results: the three cohorts comprised 1895, 1233 and 1316 participants (respective mean ages 70.1, 71.0 and 80.4 years). Statistical models explained between a fifth to a third of the variation in 25(OH)D. Supplement use and global solar radiation were positive predictors of 25(OH)D in all cohorts whereas the only universal negative predictor was body mass index. Supplement use was associated with a mean increase in 25(OH)D of between 21.4 and 35.4 nmol/l. The other main predictors varied by cohort but included sun holiday travel, enjoyment of sunshine when outside, use of vitamin D fortified milk, smoking, oily fish and egg consumption and physical frailty.
Conclusion: supplement use was the most important determinant of vitamin D status. Vitamin D fortified milk and spending time in the sun, even in the oldest old may also be useful strategies to improve 25(OH)D.

Keywords: *vitamin D, older adults, supplements, older people*

Introduction

Vitamin D deficiency is prevalent in Northern Europe affecting up to 50% or more of older adults [1, 2]. In locations at high latitude such as Ireland (52°N), little or no cutaneous synthesis occurs during the Winter months [3]. Older adults are at particular risk for deficiency for a number of reasons. Despite similar sun exposure, vitamin D production is reduced by up to 75% due to reduced epidermal concentrations of 7-dehydrocholesterol [4, 5]. Other factors including adiposity, reduced sun exposure and dietary vitamin D intake also negatively affect 25-hydroxyvitamin D [25(OH)D] status [6]. The contribution of these and other biological, dietary and lifestyle factors may vary significantly with age.

A knowledge of determinants of 25(OH)D may help identify those at risk of deficiency and inform strategies aimed at improving vitamin D status. This is important as optimisation of 25(OH)D may reduce falls and fracture risk in older adults [7, 8]. In addition, an increasing body of evidence supports a role for vitamin D in cognition, cardiovascular, neurological and autoimmune disease, as well as cancer and depression [9–11]. We aimed to investigate the determinants of 25(OH)D in the largest study to date of community dwelling older and frail Irish adults, and in particular to examine the effect of supplement use and surrogate markers of sun exposure.

Methods

The study population comprised participants of the TUDA (Trinity, Ulster, Dept. of Agriculture) study (see Figure 1). This is a large cross-sectional study designed to create a phenotype/genotype database for three cohorts of community dwelling non-institutionalised adults aged over 60 years. Recruitment started in Dec 2008 and was completed in Sept 2012. Subjects who were able to provide consent and scored ≥16 in the Mini Mental State Examination (MMSE) were eligible. Those with MMSE scores <24 were excluded in our study as we aimed to examine these relationships in non-dementia subjects.

Two cohorts (cognitive and bone) were recruited from the outpatient services at the Department of Medicine for the Elderly at St. James's Hospital, Dublin. Subjects in the cognitive cohort were recruited from geriatric clinics and a day hospital service and had cognitive impairment based on testing with the RBANS (Repeatable Battery for the Assessment of Neuropsychological Status) [12]. Subjects in the bone cohort had a diagnosis of osteoporosis or osteopaenia (within 3 years of recruitment) as defined by standard WHO criteria (T score of ≤ −2.5 and ≤ −1.0 to > −2.5 respectively) and were recruited from a specialist bone health service. The hypertensive cohort comprised subjects who had a current diagnosis of hypertension verified by their GP's and were recruited from general practices in the catchment area of the Western and

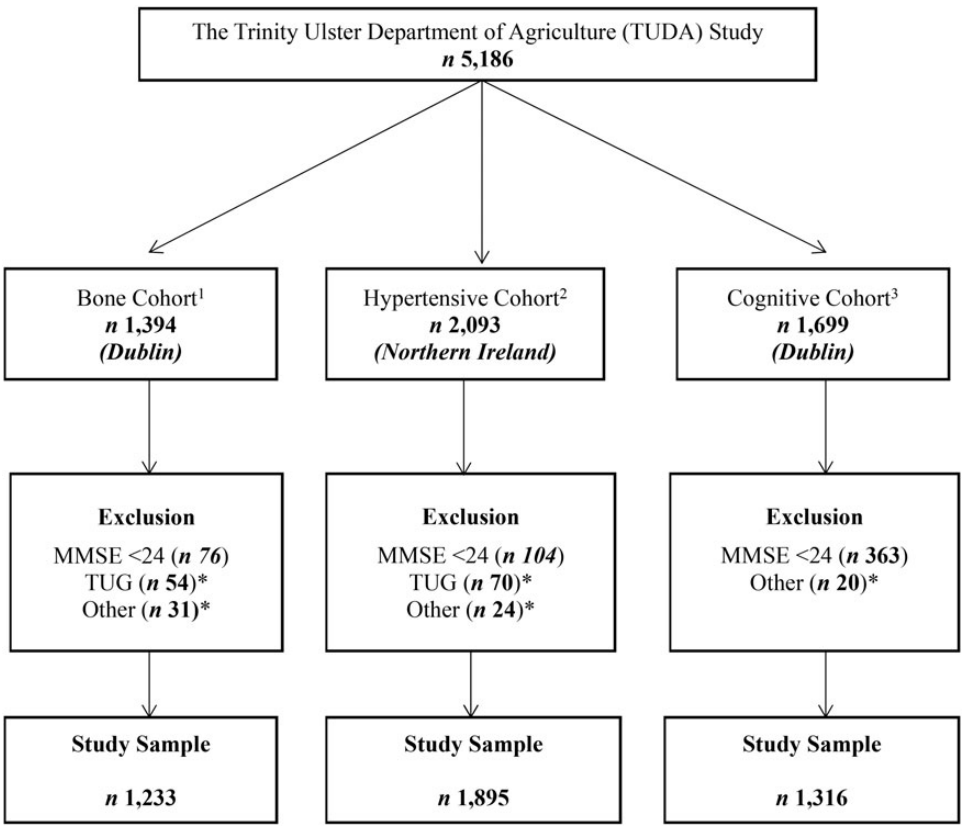

Figure 1. TUDA study population. 1. Recruitment of the Bone cohort was from specialist bone health service at St. James' Hospital, Dublin. 2. Recruitment of the hypertensive cohort was from GP clinics in Northern Ireland. 3. Recruitment of the cognitive cohort was from St. Jame's Hospital, Dublin. *Missing or incomplete data.

Northern Health and Social Care Trusts in Northern Ireland. Subjects were assessed on the day of their outpatient attendance or retrospectively and were contacted by telephone in advance and sent study information by post. All participants provided written consent and ethical approval was obtained from Research Ethnic committees. Trained researchers and doctors did study assessments.

Overview of assessments

All participants underwent a single assessment lasting about 70 min which included an interview recording self-reported information (demographic details, medical and psychosocial history, and current medications). All interviews were conducted face to face in the hospital outpatient department with or without the presence of a family member. Biophysical, cognitive assessments and functional scales were also applied.

Lifestyle factors

Subjects reported on the current use of vitamin D supplements (defined as prescribed and the over the counter vitamin D or cod liver/fish oil). The frequency of consumption of food sources of vitamin D including oily fish, eggs, vitamin D fortified milk and margarine was recorded. Smoking and alcohol history, sun holiday travel and preference for sunshine exposure and sunscreen use were also recorded.

Biophysical measures

Weight was measured with a calibrated scale accurate to 0.01 kg and height with a stadiometer (to the nearest 0.01 m). Body mass index (BMI) was calculated as per standard definition (weight/height^2). The Timed Up and Go (TUG) was measured, representing the time it takes to get out of a chair, walk three metres, turn around and walk back to return to an original seated position [13].

Non-fasting blood samples for 25(OH)D were taken on the day of assessment or within the following week. Bloods were processed on the same day and centrifuged within 3 h. 25(OH)D samples were stored at −70°C and batched for later analysis at the biochemistry laboratory at St James's Hospital, Dublin, a participant of the Vitamin D External Quality Assessment Scheme (DEQAS). 25(OH)D were measured by liquid chromatography mass spectroscopy (LCMS) using a standardised assay (Mass Chrom®) and National Institute of Standards and Technology (NIST) vitamin D standard reference material. The inter and intra-assay coefficient of variation were 5.7 and 4.5%.

Statistical analysis

All parameters were inspected for normality and normal assumptions for linear regression analysis including non-collinearity were observed. All statistical analysis was performed using JMP Edition 11.0 (SAS Institute, 2013). Statistical significance was accepted when $P < 0.05$. The sum of total global solar radiation (GSR) in the month and preceding 2 months of subject recruitment was used as a surrogate marker of UVB exposure. GSR represents the total amount of solar irradiation (direct beam plus the diffuse component on a horizontal surface) received per unit area per month. Data were obtained from the Irish Meteorological Service using weather stations nearest to study sites: Dublin Airport and Malin Head, Donegal.

Differences in cohort characteristics and 25(OH)D were explored with the one-way ANOVA, unpaired t and χ^2 test as appropriate. Cohorts were analysed separately as they had significantly different characteristics that had the potential to alter the influence of factors affecting 25(OH)D. In addition, one was also in a different geographical location. Vitamin D deficiency was defined as a 25(OH)D level below 50 nmol/l as used in other studies [2, 6]. Vitamin D supplement use included using one or more supplements listed in Supplementary data, Table S1, available in *Age and Ageing* online but excluded the use of 1α-hydroxylated vitamin D. Potential confounders were explored in a stepwise forward regression with a P-value to enter of 0.25 and to leave of 0.10. All covariates that were initially included were factors known to or have the potential to affect vitamin D status based on current literature These included age, gender, GSR, BMI, supplement use (yes/no), sunscreen use classified as no (if rarely or never), and yes (if sometimes, usually or always), sun holiday travel in last 6 months (yes/no), TUG (quintiles), preference for sunshine when outside (enjoy sunshine versus avoid sunshine), education (years), smoking status (current) versus (past or never), alcohol drinking status (yes/no) and consumption of eggs (≥3 versus <3 times per week), oily fish (≥1 versus <1 per week), vitamin D fortified milk (yes/no) and margarine (yes/no). Those variables identified as significant were then included in a final model with fixed covariates (age, gender, GSR, BMI and supplement use) as used in other studies [1, 14, 15]. The relationship between 25(OH)D and GSR was also examined by supplement use.

Results

There were 2093, 1699 and 1394 participants recruited into the hypertensive, cognitive and bone cohorts respectively. After applying inclusion criteria and allowing for missing or incomplete data, the final number of available participants for analysis in the hypertensive, cognitive and bone cohort were 1895, 1316 and 1233 (see Figure 1).

There were significant differences between cohorts as outlined in Supplementary data, Table S1 (see Supplementary data). Cognitive cohort subjects were ∼10 years older (mean age 80.4) and had more falls, physical, cognitive and functional impairment. Their mean TUG was approximately twice that of the other two cohorts (21.5 s) representing a group who are physically frail.

Vitamin D deficiency

The prevalence of vitamin D deficiency (<50 nmol/l) in non-supplemented subjects were 43.4, 66.0 and 75.0% in the

respective bone, hypertensive and cognitive cohorts. Severe deficiency (<25 nmol/l) was most prevalent (32.8%) in non-supplemented cognitive cohort participants. The mean difference in 25(OH)D due to supplementation was between 21.4 and 35.4 nmol/l ($P < 0.001$) (see Table 1).

The determinants of 25(OH)D in each cohort are shown in Table 2. Some covariates were eliminated after stepwise regression or excluded if their proportion in cohorts were too small. Overall, the models explained 29.0, 17.0 and 36.0% of the variation in 25(OH)D in the hypertensive, bone and cognitive cohorts.

Supplement use was the most important and positive predictor of 25(OH)D in all cohorts ($P < 0.0001$), whereas BMI was a negative predictor ($P \leq 0.0001$). GSR predicted higher vitamin D status in all cohorts ($P < 0.05$). The relationship with GSR was significant in supplemented subjects apart from those in the cognitive cohort. Peak GSR occurred in the month of July with peak 25(OH)D occurring around August, representing a lag period of ~1 month (see Figure 2). Sun holiday travel in the bone and hypertensive cohorts ($P < 0.0001$) was the second most important and positive predictor while current smoking in both was a negative predictor ($P = 0.030$, $P < 0.0001$). Those who enjoyed sunshine when outside were more likely to have higher 25(OH)D in the hypertensive ($P < 0.0001$) and cognitive cohorts ($P = 0.0015$) as did those who used sunscreen ($P < 0.0001$, $P = 0.023$). Consumption of fortified milk predicted higher 25(OH)D in the bone ($P = 0.001$) and cognitive cohort ($P < 0.0001$). However, no significant relationship was identified with fortified margarine. The effects of other dietary factors were inconsistent though eating eggs ≥3 times per week ($P = 0.017$) and oily fish at least once per week ($P = 0.028$) predicted higher 25(OH)D in the respective hypertensive and bone cohorts.

An independent inverse association with TUG was confined to cognitive cohort participants ($P < 0.0001$). In the hypertensive cohort female gender predicted lower 25(OH)D ($P = 0.005$) whereas increasing age predicted higher status ($P = 0.01$). Finally, no relationship with drinking or education status was identified.

Table 1. Vitamin D status in different cohorts

	Hypertensive ($n = 1895$)	Bone ($n = 1233$)	Cognitive ($n = 1316$)	*P*-value
Mean 25(OH)D nmol/l	45.6 ± 23.5[a]	60.6 ± 32.1[a]	38.2 ± 22.9[a]	<0.001[d]
	67.0 ± 27.1[b]	82.5 ± 26.8[b]	73.6 ± 29.5[b]	<0.001[d]
Difference due to supplement	21.4[c]	21.9[c]	35.4[c]	
(<25 nmol/l, %)	17.2[a]	8.6[a]	32.8[a]	<0.001[e]
	3.0[b]	1.4[b]	4.4[b]	<0.001[e]
(<30 nmol/l, %)	27.3[a]	13.8[a]	43.6[a]	<0.001[e]
	6.4[b]	3.0[b]	6.5[b]	<0.001[e]
(<50 nmol/l, %)	66.0[a]	43.4[e]	75.0[a]	<0.001[e]
	33.2[b]	10.5[b]	22.9[b]	<0.001[e]
(50–74.9 nmol/l, %)	22.3[a]	29.8[a]	16.8[a]	<0.001[e]
	35.8[b]	27.3[b]	29.6[b]	<0.001[e]

[a]Unsupplemented.
[b]Supplemented.
[c]Unpaired *t*-test, $P < 0.001$.
[d]ANOVA test.
[e]χ^2 test.

Table 2. Determinants of serum 25(OH)D in cohorts (in multiple linear regression models)

	Hypertensive ($n = 1895$) $R^2 = 0.29$		Cognitive ($n = 1316$) $R^2 = 0.36$		Bone ($n = 1233$) $R^2 = 0.17$	
	β	*P*-value	β	*P*-value	β	*P*-value
Age (years)*	0.22	0.010	0.01	0.91	0.03	0.76
Gender (female)*	−1.80	0.005	1.46	0.062	1.66	0.15
BMI (kg m^{-2})*	−0.71	<0.0001	−0.53	0.0001	−0.81	<0.0001
GSR (kJ m^{-2})*	1.22	<0.0001	0.59	<0.0001	0.32	0.048
Supplement use*	9.94	<0.0001	16.9	<0.0001	9.8	<0.0001
Current smoker*	−3.34	<0.0001	–	–	−3.35	0.030
Enjoy sunshine*	3.38	<0.0001	2.78	0.0015	–	–
Sun holiday*	7.00	<0.0001	–	–	4.29	<0.0001
Sunscreen*	1.60	<0.0001	2.00	0.023		
Vit D fortified milk*	–	–	4.10	<0.0001	2.7	0.001
Vit D fortified margarine	–	–	1.27	0.084	−1.5	0.059
Oily fish*			–	–	1.7	0.028
Eggs*	1.58	0.017	–	–	–	–
Timed up and Go (TUG)*	–	–	−2.22	<0.0001	–	–
Education (years)	–	–	–	–	–	–
Current drinker	–	–	–	–	–	–

BMI, body mass index; GSR, global solar radiation; TUG, Timed Up and Go; –, not included in model as proportion of covariate too low or excluded after stepwise regression (*P*-value to enter 0.25 and to leave 0.10).
*Statistically significant in any cohort ($P < 0.05$) after adjustment with other covariates in model.

Discussion

In our analysis of three cohorts of community dwelling older Irish adults, we identified factors that explained between approximately one-fifth to one-third of the total variation in 25(OH)D. Positive predictors of 25(OH)D in all cohorts were vitamin D supplement use and GSR whilst the only universal negative determinant was BMI. The relationship with dietary and other factors including physical frailty, smoking, gender and sun exposure habits was inconsistent.

Vitamin D supplement use as expected was the most important predictor of 25(OH)D. The observed unadjusted effect was +21.4 nmol/l, +21.9 nmol/l and +35.4 nmol/l in the respective hypertensive, bone and cognitive cohorts. These differences are similar to a mean difference of 23.8 nmol/l attributed to supplement use in 546 community dwelling Irish adults [14]. The greater effect in the bone and cognitive cohort may be explained by the majority taking prescribed supplements (ideas™, calcichew™ and osteofos™) which may contain more vitamin D (typically 800 IU per day). The prevalence of vitamin D deficiency (<50 nmol/l) was high in unsupplemented subjects ranging from 43.4 to 75.0% in the older and frailer cognitive cohort.

GSR was positively associated with 25(OH)D in all cohorts consistent with a recent study showing a positive correlation between 25(OH)D and 3 month solar UV-B irradiance [16]. The relationship remained significant in supplemented subjects

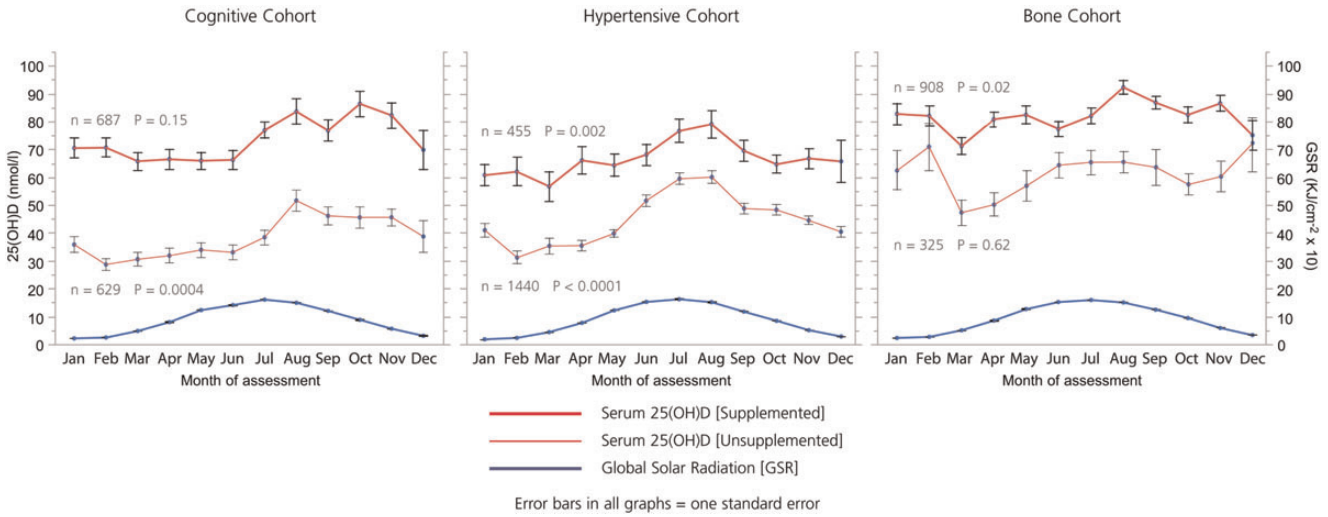

Figure 2. Graph to show serum 25(OH)D versus month and global solar radiation. *P*-value for significance of relationship between serum 25(OH)D and global solar radiation (GSR) after adjusting for age, gender and body mass index.

(except in the cognitive cohort) where supplement use may be marker of greater frailty and less sun exposure. A previous study of older Irish adults found no association with monthly GSR in those who were supplemented [14]. However, our sample size was larger and we used GSR data over a 2 to 3-month period. The lack of association with GSR in non-supplemented subjects in the bone cohort might relate to the small sample size. 25(OH)D levels were lowest in the Spring and highest in the Autumn months similar to other studies of older European adults [2, 15].

Similar to other studies, enjoying sunshine when outdoors predicted higher 25(OH)D in the cognitive and hypertensive cohorts as did sun holiday travel where explored [15, 17]. The high level of supplement use in the bone cohort may have diminished the effect of sun exposure. Sunscreen use unexpectedly predicted higher 25(OH)D in the hypertensive and cognitive cohorts but may be a surrogate marker of greater sun exposure as previously suggested [15, 17].

BMI was a universal negative predictor of 25(OH)D in keeping with most previous studies [1, 18]. Sequestration of 25(OH)D in fat cells may accounts for this finding, though it may also be involved in cell signalling pathways that could lead to an increased risk of obesity through increased lipogenesis [19]. Unexpectedly, increasing age predicted higher 25(OH)D in the hypertensive cohort. However, the lack of an inverse relationship may relate to the relatively narrow age range of participants in all three cohorts. The association with gender was inconsistent in keeping with other studies [20]. Current smoking was a negative predictor of 25(OH)D in both the bone and hypertensive cohorts as previously reported [1, 21]. Alterations in hepatic metabolism of vitamin D or 1-α-hydroxylation due to smoking could be a potential mechanism [22]. Alternatively, smoking may be a surrogate marker for adverse diet and lifestyle factors that diminish 25(OH)D such as lower vitamin D intake [23].

Fortified margarine had no effect on 25(OH)D but this is not surprising given the small amount consumed and its low vitamin D content. Conversely, fortified milk was a positive predictor of 25(OH)D in the bone and cognitive cohort. Fortified milk mainly constituted Supermilk© which contains about 80 IU of vitamin D3 per 200 ml. Few studies have examined the effect of fortified milk in older adults, though a small intervention trial did find a beneficial effect on 25(OH)D in older Irish subjects [24]. Consumption of oily fish at least once per week in the bone cohort and eggs ≥3 times per week in the hypertensive cohort were also predictors of better 25(OH)D status, a result previously reported by other studies [15, 25]. However, these factors may be surrogate markers of better health and compliance with supplement use.

Lower 25(OH)D was also an independent predictor of physical frailty (as measured by TUG) but only in cognitive cohort participants who had a higher prevalence of deficiency and were frailer. Few studies have explored the association between 25(OH)D and TUG, though an inverse relationship has been found in community dwelling adults aged 70 years or older [26, 27]. Other studies in older adults identified no association with physical frailty but used more specific measures [28]. Reduced UVB exposure in those who are frail may account for any relationship. However, low 25(OH)D status might directly lead to frailty as deficiency has been associated with myopathy and supplementation has been found to improve performance in the TUG and other physical measures in older adults [29].

Our study strengths included its large size with subjects from widely varying ages, exclusion of those likely to have dementia and our accurate account of vitamin D supplement use. We also adjusted for a several factors related to UVB exposure and measured 25(OH)D by LCMS. However, we did not have adequate measures of non-supplemental dietary vitamin D intake, outdoor exposure or physical activity. In particular, we were not able to accurately account for meat consumption which is the main contributor to dietary vitamin D intake in Ireland [30]. However, apart from supplements, the overall contribution of diet to vitamin D status is small and unlikely to significantly alter our results.

In summary, supplement use, GSR and sun holiday travel were positive predictors of 25(OH)D while BMI, smoking and other factors negatively influenced status. We identified that those at most risk of deficiency were unsupplemented, oldest and frail in which prevalence was high at 75%. However, even in such a group, fortified milk consumption and spending time outdoors in the sun, might be practical strategies to improve 25(OH)D.

Key points

- Supplement use was the most important determinant of vitamin D status (mean increase in 25(OH)D of between 21.4 and 35.4 nmol/l).
- Physical frailty as assessed by the Timed up and Go was inversely associated with 25(OH)D but only in 'older' old adults.
- Vitamin D fortified milk and spending time in the sun, even in the 'oldest' old may be useful strategies to improve 25(OH)D.

Conflicts of interest

K.M. received an honorarium for his input on a Vitamin D advisory panel for Consilient Health Ltd, Ireland.

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Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

References

1. Hirani V, Tull K, Ali A, Mindell J. Urgent action needed to improve vitamin D status among older people in England! Age Ageing 2010; 39: 62–8.
2. Klenk J, Rapp K, Denkinger MD *et al*. Seasonality of vitamin D status in older people in Southern Germany: implications for assessment. Age Ageing 2013; 42: 404–8.
3. 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.
4. MacLaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. J Clin Invest 1985; 76: 1536–8.
5. Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet. Lancet 1989; 2: 1104–5.
6. Holick MF. Vitamin D deficiency. N Engl J Med 2007; 357: 266–81.
7. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB *et al*. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ 2009; 339: b3692.
8. Bischoff-Ferrari HA, Willett WC, Orav EJ *et al*. A pooled analysis of vitamin D dose requirements for fracture prevention. N Engl J Med 2012; 367: 40–9.
9. Wacker M, Holick MF. Vitamin D—effects on skeletal and extraskeletal health and the need for supplementation. Nutrients 2013; 5: 111–48.
10. Anglin RE, Samaan Z, Walter SD, McDonald SD. Vitamin D deficiency and depression in adults: systematic review and meta-analysis. Br J Psychiatry 2013; 202: 100–7.
11. DeLuca GC, Kimball SM, Kolasinski J, Ramagopalan SV, Ebers GC. Review: the role of vitamin D in nervous system health and disease. Neuropathol Appl Neurobiol 2013; 39: 458–84.
12. Randolph C, Tierney MC, Mohr E *et al*. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): preliminary clinical validity. J Clin Exp Neuropsychol 1998; 20: 310–9.
13. Podsiadlo D, Richardson S. The timed 'Up & Go': a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991; 39: 142–8.
14. Romero-Ortuno R, Cogan L, Browne J *et al*. Seasonal variation of serum vitamin D and the effect of vitamin D supplementation in Irish community-dwelling older people. Age Ageing 2011; 40: 168–74.
15. Hyppönen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. Am J Clin Nutr 2007; 85: 860–8.
16. Greenfield JA, Park PS, Farahani E *et al*. Solar ultraviolet-B radiation and vitamin D: a cross-sectional population-based study using data from the 2007 to 2009 Canadian Health Measures Survey. BMC Public Health 2012; 12: 660.
17. Mavroeidi A, Aucott L, Black AJ, Fraser WD, Reid DM, Macdonald HM. Seasonal variation in 25(OH)D at Aberdeen (57°N) and bone health indicators—could holidays in the sun and cod liver oil supplements alleviate deficiency? PLoS One 2013; 8: e53381.
18. Saneei P, Salehi-Abargouei A, Esmaillzadeh A. Serum 25-hydroxy vitamin D levels in relation to body mass index: a systematic review and meta-analysis. Obes Rev 2013; 14: 393–404.
19. vinh quoc Lu'o'ng K, Nguyen LT. The beneficial role of vitamin D in obesity: possible genetic and cell signaling mechanisms. Nutr J 2013; 89: 2891–12–89.
20. Hilger J, Friedel A, Herr R, Rausch T *et al*. A systematic review of vitamin D status in populations worldwide. Br J Nutr 2013; 111: 1–23.
21. Cutillas-Marco E, Fuertes-Prosper A, Grant WB, Morales-Suarez-Varela M. Vitamin D deficiency in South Europe: effect of smoking and aging. Photodermatol Photoimmunol Photomed 2012; 28: 159–61.
22. Brot C, Jorgensen NR, Sorensen OH. The influence of smoking on vitamin D status and calcium metabolism. Eur J Clin Nutr 1999; 53: 920–6.
23. Morabia A, Bernstein MS, Antonini S. Smoking, dietary calcium and vitamin D deficiency in women: a population-based study. Eur J Clin Nutr 2000; 54: 684–9.

24. Keane EM, Healy M, O'Moore R, Coakley D, Walsh JB. Vitamin D-fortified liquid milk: benefits for the elderly community-based population. Calcif Tissue Int 1998; 62: 300–2.
25. Nakamyra K, Nashimoto M, Hori Y, Yamamoto M. Serum 25-hydroxyvitamin D concentrations and related dietary factors in peri- and postmenopausal Japanese women. Am J Clin Nutr 2000; 71: 1161–5.
26. Dukas L, Staehelin HB, Schacht E, Bischoff HA. Better functional mobility in community-dwelling elderly is related to D-hormone serum levels and to daily calcium intake. J Nutr Health Aging 2005; 9: 347–51.
27. Kwon J, Suzuki T, Yoshida H, Kim H, Yoshida Y, Iwasa H. Concomitant lower serum albumin and vitamin D levels are associated with decreased objective physical performance among Japanese community-dwelling elderly. Gerontology 2007; 53: 322–8.
28. Matheï C, Van Pottelbergh G, Vaes B, Adriaensen W, Gruson DDegryse JM. No relation between vitamin D status and physical performance in the oldest old: results from the Belfrail study. Age Ageing 2013; 42: 186–90.
29. Rejnmark L. Effects of vitamin D on muscle function and performance: a review of evidence from randomised controlled trials. Ther Adv Chronic Dis 2011; 2: 25–37. (6):407–14.
30. Cashmann KD, Seamans KM, Lucey AJ *et al*. Relative effectiveness of oral 25 hydroxyvitamin D3 in raising wintertime serum 25-hydroxyvitamin D in older adults. Am J Clin Nutr 2012; 95: 1350–6.

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Antibiotic prescribing and associated diarrhoea: a prospective cohort study of care home residents

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Abstract

Background: the risk factors for and frequency of antibiotic prescription and antibiotic-associated diarrhoea (AAD) among care home residents are unknown.
Aim: to prospectively study frequency and risks for antibiotic prescribing and AAD for care home residents.