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Official Journal of the Irish Medical Organisation

Ir Med J; September 2026; Vol 119; No. 8; P152
28th September, 2026
Original Paper

Vitamin D Testing Deviations in General Internal Medicine Inpatients

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Abstract

Aims

To evaluate adherence to Health Service Executive (HSE) criteria, identify predictors of testing deviations, and assess the clinical management of vitamin D results in a general internal medicine (GIM) inpatient cohort.

Methods

A retrospective review of 408 GIM inpatients categorised into four groups based on HSE-defined testing appropriateness: (1) testing indicated and ordered, (2) indicated but not ordered, (3) not indicated but ordered, and (4) not indicated and not ordered. Testing appropriateness was assessed against HSE Lab criteria, and predictors of testing practices and vitamin D levels were analysed using logistic regression models in R statistical software (v4.1.2), adjusted for age, gender, ethnicity, and hospital length of stay.

Results

Of 408 patients, 143 (35%) deviated from guidelines: 91 (22.3%) lacked indicated testing, while 50 (12.3%) underwent unindicated tests. Older age (OR 1.08 per year, 95% CI 1.04–1.13; p<0.001) and prolonged hospitalisation (OR 1.01 per day, 95% CI 1.00–1.01; p=0.03) predicted testing regardless of indication. Of 77 tested patients, 48 (62.3%) had sufficient levels (≥50 nmol/L), 13 (16.9%) insufficient (30–49 nmol/L), and 16 (20.8%) deficient (<30 nmol/L).

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Discussion
Deviations from HSE Lab criteria were frequently observed, with older patients overtested and high-risk populations undertested.

Introduction

Vitamin D is a fat-soluble vitamin found in many forms in the human body. The skin, liver and kidneys synthesize its active form, 1,25-hydroxyvitamin D3 (1,25-OH D). This active form serves as the ligand for the vitamin D receptor (VDR), which is expressed in nearly every organ system of the body.[1] The importance of vitamin D is well described in musculoskeletal development and function. Deficiency or impaired conversion leads to classical, skeletal manifestations such as osteomalacia or rickets.[2] Evidence is emerging that vitamin D deficiency may have extra-skeletal effects, the most prominent of which may be the effect on the cardiovascular system. Clinically, an inverse association between vitamin D levels and cardiovascular disease is suggested.[3] Furthermore, an association between vitamin D deficiency and all-cause mortality, including cancer mortality, has been proposed.[4,5] However, it is recognised that associations found between vitamin D deficiency and health conditions may not be causal due to multiple confounding variables.[6]

Testing of vitamin D levels may be important in determining deficiency and its consequences on human health. The active metabolite of vitamin D is 1,25-OH D, however, 25-hydroxyvitamin D3 (25-OH D) is the form most used to assess vitamin D status in clinical studies and patient care.[1] In Ireland, the Health Service Executive (HSE) advises against routine vitamin D testing in healthy individuals, recommending it only for specific clinical indications such as metabolic bone disease, malabsorption, chronic inflammatory conditions, or use of certain medications.[7] Testing is not required for general screening, pregnancy, or healthy children, where supplementation should instead be provided: 10 micrograms/day during pregnancy and winter, and 5 micrograms/day for infants. Repeat testing should be performed within six months unless clinically justified.[7,8] This strategy helps reduce unnecessary testing, optimizes resource allocation, and encourages appropriate supplementation across the population.

Systematic reviews indicate that over 50% of the world's population may have suboptimal vitamin D concentrations,[9] which may give weight to exploring the importance of supplementation worldwide. Vitamin D supplementation is suggested to be a promising strategy with preventative effects on diseases, including hypertension, type 2 diabetes and cardiovascular events.[5,10] Supplementation may have significant implications on mental and

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cognitive health, with potential positive effects on reducing the development and symptoms of depression and Alzheimer's disease.[5,11] Novel evidence has emerged that supplementation may also have effects on autoimmunity, with Thouvenot et al.[12] demonstrating reduced disease activity in clinically isolated syndrome and relapsing-remitting multiple sclerosis. In Ireland, it is recommended that teenagers and adults aged less than 65 years take 15 micrograms of vitamin D3 daily from Halloween (31st October) to St. Patrick's Day (17th March) every year. It is recommended that adults older than 65 years take 15 micrograms daily throughout the year.[13]

Despite available guidelines, studies report widespread overtesting in low-risk groups and undertesting in indicated cases.[14,15] This study aims to evaluate adherence to HSE criteria,[7] identify predictors of testing deviations, and assess the clinical management of vitamin D results in a general internal medicine (GIM) inpatient cohort.

Methods

This was a retrospective study of anonymised, routinely collected clinical data and did not involve prospective patient recruitment, randomisation, or intervention. In accordance with the Health Research Regulations 2018 (Ireland) and institutional guidelines, formal Research Ethics Committee approval was not required. The study was reviewed, approved, and registered with the Clinical Audit Office at our institute (Reference No: 78, dated November 12th, 2024). All data were fully de-identified prior to analysis and handled in compliance with GDPR and hospital data protection policies

This retrospective, cross-sectional study evaluated the appropriate practice of vitamin D level testing and management. The study population consisted of inpatients who were discharged from a GIM service in a large acute academic teaching hospital in Ireland between 21st July 2024 and 21st August 2024. Exclusion criteria for this study were: 1) age <18 years; 2) inpatient stay <24 hours. The patients were categorised into four groups based on HSE Laboratory Guideline Criteria[7]: 1) vitamin D testing indicated and ordered; 2) vitamin D testing indicated but not ordered; 3) vitamin D testing not indicated but ordered; 4) vitamin D testing not indicated and not ordered.

All information was sourced from the hospital database via electronic patient records (EPR). We extracted demographic (age, gender, ethnicity), clinical (length of stay, pre-admission vitamin D supplementation), background conditions and vitamin D level from EPR. Two independent physicians used HSE criteria to adjudicate testing appropriateness, and a third reviewer resolved discrepancies. All data was anonymised and kept in a dedicated password-protected datasheet.

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We analysed all data in the R statistical programming language and the finalfit package.[16] We fitted a logistic regression model to identify predictors of appropriate vitamin D management, and a linear regression model to identify predictors of vitamin D level. Both models controlled for age, gender, ethnicity, and hospitalisation duration.

Results

Appropriateness of Vitamin D Testing

Of 408 general internal medicine (GIM) inpatients, 35% (n=141) demonstrated inappropriateness of vitamin D testing. Testing was not indicated but ordered in 12.3% (n=50) of cases, while indicated testing was omitted in 22.3% (n=91) (Table 1). Only 6.6% (n=27) of patients received appropriately indicated testing.

Demographic and Clinical Characteristics by Testing Group

Demographic analysis revealed differences across groups. Patients undergoing unindicated testing were older (mean age 79.5 vs. 57.9 years in the "not indicated/not ordered" group) and had longer hospital stays (mean 30.8 days vs. 10.2 days) (Table 2). Logistic regression found no significant predictors of testing being indicated (supplementary table 1).

Older age (OR 1.08 per year, 95% CI 1.04–1.13, p=0.001) was associated with a higher likelihood of testing being ordered, regardless of indication (Table 3).

Management of Vitamin D Results

Of 77 tested patients, 62.3% (48) had sufficient levels (≥50 nmol/L), 16.9% (13) insufficient (30–49 nmol/L), and 20.8% (16) deficient (<30 nmol/L). Supplementation was omitted in 32/48 (66.7%) patients with adequate levels who required maintenance therapy (Table 4).

Patients with insufficient vitamin D levels were less likely to receive appropriate management as compared to patients with adequate vitamin D levels (OR 0.25, 95% CI 0.09–0.69, p=0.008). Increased age was also associated with appropriate vitamin D management (OR 1.03 per year, 95% CI 1.00–1.06, p=0.058) (Table 5).

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Predictors of Vitamin D Levels

Pre-admission vitamin D supplementation was strongly associated with higher vitamin D levels (β=24.84 nmol/L, 95% CI 14.04–35.65, p<0.001) after adjustment for age, gender, and ethnicity. Unadjusted analyses suggested older age correlated with higher levels (β=0.50 per year, 95% CI 0.09–0.91, p=0.018), but this association was not statistically significant at the 95% confidence level after multivariable adjustment. Women had a higher mean vitamin D level than men, although this was not statistically significant after multivariable regression (β=0.29 per year, 95% CI -0.09–0.68, p=0.135) (Supplementary Table 2).

Patients with adequate vitamin D levels were more likely to have received pre-admission supplementation (85.5%, 53) compared to those with deficient levels (4.8%, 3) (Table 6).

Discussion

There was a 35% deviation from the HSE Lab Criteria for vitamin D testing.[7] Of this 35%, 22.3% represented situations where testing was indicated but not carried out. This contrasts with existing literature, which shows considerable over-testing for vitamin D levels. Woodford et al.[14] propose that 70% of tests could be inappropriate in a healthcare setting. In 2023, an Irish study reported that 53% of tests were not indicated.[15] Our findings may demonstrate increased adherence to existing guidelines, with only 12.3% of ordered tests falling outside recommended indications.

In our study, older age was associated with a higher likelihood of vitamin D levels being ordered regardless of indication. Patients who underwent inappropriate testing were more likely to be older, with a mean age of 79.5 years. The HSE guidelines not including age and frailty as indications for testing aligns with most international standards, with many expressly advising against routine testing in these populations.[7] The proposed reasoning against routine testing in older aged patients is that empiric vitamin D supplementation is recommended for those aged over 65 years,[13] and therefore testing is unnecessary and costly.[7]

Both under-testing for Vitamin D deficiency and testing when not indicated occurred in our study. The deviation in testing practice from HSE guidelines may have been largely driven by increased testing in older adults and those with prolonged hospital stays. These findings align with prior research highlighting age-related biases in diagnostic practices. Older patients often receive more investigations, even when clinical indications are unclear, potentially due to concerns about frailty or undifferentiated symptoms such as fatigue and falls.[2,4] However, age and prolonged hospitalisation are not recognised criteria for testing under current HSE guidelines,[7] indicating a gap between policy and clinical practice. Previous research has

identified that the most common major barriers to guideline adherence include complexity of guideline documents, a high number of weak or conditional recommendations, and time constraints due to competing clinical responsibilities.[18]

Our findings showed a strong association between pre-admission vitamin D supplementation and adequate serum levels at the time of hospitalisation. Patients who had been taking supplements before admission were significantly more likely to have sufficient vitamin D levels ($p < 0.001$), consistent with previous studies demonstrating the value of routine supplementation in older adults.[6,13]

The majority (66.7%) of patients with adequate levels of vitamin D were not commenced on appropriate maintenance vitamin D supplementation as per current HSE guidelines.[7] This aligns with previous data showing that barriers to widespread supplementation remain, including limited awareness of guidelines for treatment among patients and prescribers, variable adherence to treatment, and inconsistent messaging about indications and dosing.[2,7] Clinician hesitancy may stem from uncertainty around benefits in asymptomatic patients or fear of over-treatment. Touskova et al.[19] demonstrated that adherence rates to vitamin D supplementation remained consistently low, with around 70% adherence at baseline and after one year.

Overtesting of vitamin D levels in the tertiary care setting is reflected in the not indicated but ordered cohort of our study population (12.3%). This cohort represents a low pre-test probability in which vitamin D testing is not clinically indicated based on current guidelines. This can result in resource wastage. Vitamin D testing is a relatively expensive endeavour with a standard 25-Hydroxyvitamin D (25-OH D) test estimated to cost €16.50 to process in the lab.[20] This contributes to laboratory burden in the hospital setting. Overtesting in the tertiary healthcare centre has been demonstrated by Araclica et al.[21] with 57% of vitamin D tests likely being avoidable expenditure, similarly Norton et al.[22] demonstrated that approximately half of vitamin D tests audited were potentially unnecessary.

Vitamin D undertesting was observed in 22.3% (indicated but not ordered) of patient population at risk of vitamin D deficiency. High risk groups, such as those with chronic kidney disease who remain undiagnosed, are impacted adversely as a result. For those with chronic kidney disease vitamin D deficiency is common, with La Clair et al.[23] demonstrating that only 29% and 17% of patients respectively with stage three and four CKD have sufficient 25 (OH)-Vitamin D levels. This vitamin D deficiency contributes to mineral and bone disorders and accelerates CKD progression.

Improving targeted care for high-risk groups may lead to economic and clinical benefits. O'Sullivan et al.[24] proposed that testing for vitamin D levels has increased exponentially in the

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period of 2000 to 2015 with an average annual increase of 54% in the UK. This leads to low value care with inefficient use of healthcare resources. Van Vugt et al.[25] in a cluster randomized intervention study, demonstrates that the education of General Practitioners (GP) on appropriate testing may lead to a reduction of 23% of vitamin D levels ordered. Ultimately, targeted testing offers a cost-effective approach that aligns with evidence-based practice.

Our methodology featured robust adjudication processes with two independent physicians applying HSE criteria and third-reviewer resolution of discrepancies. We analysed comprehensive electronic health records across a substantial inpatient cohort (408), controlling for key demographic and clinical variables in regression models.

The single-centre design limits generalizability due to potential institutional biases. The small sample size of vitamin D deficient cases reduced statistical power for analysing severe deficiency outcomes.

This study demonstrates persistent gaps in vitamin D management. Undertesting of those at risk of deficiencies can occur, which may lead to missed opportunities to optimise patient health. Vitamin D level testing when not indicated has also been shown to occur, with older age and prolonged hospital stay being possible risk factors for unnecessary testing. Future initiatives should focus on guideline implementation, clinician education, and system-level interventions to optimise vitamin D stewardship.

Declarations of Conflicts of Interest:
None declared.

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Appendix:

Table 1: Appropriateness of Vitamin D Testing

Phenotype	**n**	**Proportion (%)**
Not indicated and not ordered	239	58.6
Indicated but not ordered	91	22.3
Not indicated but ordered	50	12.3
Indicated and ordered	27	6.6

n-number, %-percentage

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Table 2: Demographic and Clinical Characteristics by Testing Group

Variable	Levels	Not Indicated/Not Ordered	Indicated/Not Ordered	Not Indicated/Ordered	Indicated/Ordered
Age (years)	Mean (SD)	57.9 (21.6)	60.0 (15.8)	79.5 (12.0)	75.3 (16.1)
Gender	Male (%)	115 (57.8)	47 (23.6)	21 (10.6)	16 (8.0)
	Female (%)	124 (59.6)	44 (21.2)	29 (13.9)	11 (5.3)
Caucasian descent	No (%)	28 (71.8)	8 (20.5)	2 (5.1)	1 (2.6)
	Yes (%)	211 (57.3)	83 (22.6)	48 (13.0)	26 (7.1)
Length of stay (days)	Mean (SD)	10.2 (33.7)	12.2 (29.5)	30.8 (66.5)	26.8 (36.8)

%-percentage, SD- standard deviation

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Table 3: Predictors of Vitamin D being ordered regardless of indication

Dependent: Vitamin D ordered		FALSE	TRUE	OR (univariable)	OR (multivariable)
Indication for screening	Not indicated (level within 6 months)	0 (NaN)	0 (NaN)	-	-
	Drugs (Glucocorticoids, Anticonvulsants, Antiretrovirals, Antifungals, Anti-Oestrogens or Cholestyramine)	31 (75.6)	10 (24.4)	-	-
	Not indicated (on supplementation)	0 (NaN)	0 (NaN)	-	-
	Not indicated (absence of indications)	0 (NaN)	0 (NaN)	-	-
	Multiple	15 (78.9)	4 (21.1)	0.83 (0.20-2.94, p=0.776)	0.92 (0.19-3.91, p=0.913)
	Chronic Inflammation	7 (100.0)	0 (0.0)	0.00 (NA-3773007237794609793805784067067644704046882247147 52.00, p=0.991)	0.00 (NA-11467942384103472318521867694233585362927616.00, p=0.991)
	Malabsorption/CKD/Liver Disease	11 (84.6)	2 (15.4)	0.56 (0.08-2.59, p=0.500)	1.04 (0.12-6.44, p=0.967)
	Osteoporosis/Osteopaenia	4 (66.7)	2 (33.3)	1.55 (0.19-9.27, p=0.641)	1.24 (0.14-8.38, p=0.831)
	Repeat (Malabsorption or low baseline)	22 (81.5)	5 (18.5)	0.70 (0.20-2.28, p=0.569)	0.50 (0.12-1.89, p=0.321)
	Pathological Fracture	0 (0.0)	2 (100.0)	131888918.26 (0.00-NA, p=0.995)	71151839.89 (0.00-NA, p=0.994)
	Unexplained Hypocalcaemia/Raised PTH/Low or High Phosphate	1 (33.3)	2 (66.7)	6.20 (0.54-142.07, p=0.153)	10.10 (0.61-287.77, p=0.111)
Age, years	Mean (SD)	60.0 (15.8)	75.3 (16.1)	1.07 (1.04-1.12, p<0.001)	1.08 (1.04-1.13, p=0.001)
Gender	M	47 (74.6)	16 (25.4)	-	-
	F	44 (80.0)	11 (20.0)	0.73 (0.30-1.74, p=0.487)	0.49 (0.16-1.45, p=0.207)
Caucasian descent	FALSE	8 (88.9)	1 (11.1)	-	-
	TRUE	83 (76.1)	26 (23.9)	2.51 (0.43-47.60, p=0.397)	0.74 (0.08-17.43, p=0.814)
LOS, days	Mean (SD)	12.2 (29.5)	26.8 (36.8)	1.01 (1.00-1.03, p=0.100)	1.01 (0.99-1.02, p=0.258)

OR = Odds Ratio; "NaN" values in logistic regression models reflect cells with zero observations, CKD- chronic kidney disease, PTH- parathyroid hormone, SD, standard deviation, LOS- length of stay, M-Male, F-Female, LOS- length of stay

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Table 4: Response to Vitamin D Levels

Vitamin D Classification	No Supplementation (No Need)	No Supplementation (Should Have Been)	No Supplementation (Already on Therapy)	Yes (Maintenance)	Yes (Loading)
Adequate	7	32	7	2	0
Insufficient	0	2	9	1	1
Deficient	0	0	9	2	5

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Table 5: Factors associated with appropriate vitamin D management.

Dependent: Appropriate management		**No**	**Yes**	**OR (95% CI, p-value) (univariable)**	**OR (95% CI, p-value) (multivariable)**
Age	Mean (SD)	74.2 (11.7)	58.5 (21.3)	0.96 (0.94-0.97, p<0.001)	1.03 (1.00-1.06, p=0.058)
Gender	M, n (%)	48 (24.1)	151 (75.9)	-	-
	F, n (%)	47 (22.6)	161 (77.4)	1.09 (0.69-1.73, p=0.716)	1.47 (0.66-3.27, p=0.341)
Vitamin D level classification	Adequate	20 (26.0)	57 (74.0)	-	-
	Insufficient	13 (59.1)	9 (40.9)	0.24 (0.09-0.65, p=0.005)	0.25 (0.09-0.69, p=0.008)
	Deficient	13 (52.0)	12 (48.0)	0.32 (0.13-0.82, p=0.018)	0.42 (0.16-1.12, p=0.082)

SD- standard deviation, M-male, F-female, n-number. %- percentage, OR- odds ratio, CI- confidence interval

Table 6: Predictors of Vitamin D

Label	Levels	Deficient	Adequate	Insufficient
Age	Mean (SD)	72.0 (14.8)	78.8 (12.8)	76.1 (15.2)
Gender	M, n (%)	17 (28.8)	31 (52.5)	11 (18.6)
	F, n (%)	8 (12.3)	46 (70.8)	11 (16.9)
Caucasian descent	TRUE	25 (20.8)	73 (60.8)	22 (18.3)
	FALSE		4 (100.0)	
Supplementation pre-admission	FALSE	22 (35.5)	24 (38.7)	16 (25.8)
	TRUE	3 (4.8)	53 (85.5)	6 (9.7)

F- female, M- male, n- number, %- percentage, SD- standard deviation

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Official Journal of the Irish Medical Organisation

Ir Med J; September 2026; Vol 119; No. 8; P152
28th September, 2026
Original Paper

Supplementary Table 1: Predictors of Vitamin D testing being indicated

Dependent: Vitamin D indicated		**FALSE**	**TRUE**	**OR (CI, p-value) (univariable)**	**OR (CI, p-value) (multivariable)**
Age	Mean (SD)	61.6 (21.9)	63.5 (17.1)	1.00 (0.99-1.02, p=0.402)	1.00 (0.99-1.02, p=0.471)
Gender	M, n (%)	136 (68.3)	63 (31.7)	-	-
	F, n (%)	153 (73.6)	55 (26.4)	0.78 (0.50-1.19, p=0.247)	0.77 (0.50-1.20, p=0.249)
Caucasian descent	FALSE	30 (76.9)	9 (23.1)	-	-
	TRUE	259 (70.4)	109 (29.6)	1.40 (0.67-3.23, p=0.394)	1.28 (0.59-3.00, p=0.548)
LOS, days	Mean (SD)	13.7 (41.9)	15.6 (31.8)	1.00 (1.00-1.01, p=0.668)	1.00 (0.99-1.01, p=0.907)

OR- odds ratios, CI- confidence interval, SD- standard deviation, n- number, %-percentage, LOS- length of stay

Supplementary Table 2: Logistic regression analysis of Vitamin D predictors

Dependent: Vitamin D level		**unit**	**value**	**Coefficient (univariable)** β (95% CI, p-value)	**Coefficient (multivariable)** β (95% CI, p-value)
Age	[35.0,97.0]	Mean (SD)	65.3 (32.4)	0.50 (0.09 to 0.91, p=0.018)	0.29 (-0.09 to 0.68, p=0.135)
Gender	M	Mean (SD)	58.8 (34.3)	-	-
	F	Mean (SD)	71.3 (29.6)	12.48 (1.12 to 23.85, p=0.032)	6.49 (-4.15 to 17.13, p=0.229)
Caucasian descent	FALSE	Mean (SD)	76.8 (18.1)	-	-
	TRUE	Mean (SD)	64.9 (32.8)	-11.81 (-44.48 to 20.86, p=0.476)	-12.71 (-42.07 to 16.66, p=0.393)
Supplementation pre-admission	FALSE	Mean (SD)	51.4 (32.7)	-	-
	TRUE	Mean (SD)	79.3 (25.5)	27.87 (17.44 to 38.31, p<0.001)	24.84 (14.04 to 35.65, p<0.001)

SD- standard deviation, M- male, F- female, β- Regression coefficient, CI- confidence interval