Feasibility of screening for and treating vitamin D deficiency in forensic psychiatric inpatients

Jill Murie MPH FRCGP MFFLM, GP, Forensic Physician and Primary Care Researcher a, *, Claudia-Martina Messow PhD , Consultant Statistician b, Bridie Fitzpatrick PhD, MSc, University Lecturer c

a NHS Scotland State Hospital and NHS Education for Scotland, 2 Central Quay, Glasgow G3 8BW, United Kingdom
b Robertson Centre for Biostatistics, Boyd Orr Building, University of Glasgow, Glasgow G12 8QQ, United Kingdom
c Nursing & Health Care School, 59 Oakfield Avenue, Glasgow, G12 8LL, United Kingdom

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Abstract
Neuroleptic and anti-epileptic medication, inadequate vitamin D intake and limited solar exposure increase the risk of vitamin D deficiency in high security psychiatric environments. Of the 33 inpatients (40% selected; 21% of hospital population) completing this cross-sectional study, 36% had insufficient and 58% deficient vitamin D. Five patients with vitamin D deficiency had secondary hyperparathyroidism, two of whom had osteopenia on dual-emission X-ray absorptiometry. At 1-year follow up, of the 31 patients eligible, 15 had accepted and continued supplements. Systematic screening is therefore necessary due to mental health and consent issues. Implications of supplementation and grounds access are discussed.

1. Introduction

Over 90% of vitamin D is produced by the skin after exposure to ultraviolet B light from the sun or other artificial sources. It also occurs naturally in a limited range of foods such as seafood, mushrooms and egg yolks. Vitamin D plays an essential role in bone and mineral metabolism, muscle function and immunity. Classically persistent vitamin D deficiency (serum 25-hydroxyvitamin D [25 OHD] < 25 mmol/L) is associated with rickets in children and osteomalacia in adults, manifested as skeletal deformity, bone pain and low trauma bone fractures. In addition, vitamin D deficiency has been associated with an increased risk of a wide range of non-skeletal and non autoimmune conditions, including all cancers and cardiovascular disease, but these associations may be confounded by other variables such as increased age, body weight and frailty. Despite this, there is some evidence from randomised controlled intervention trials to suggest that vitamin D insufficiency may be a marker of greater morbidity.

Secondary hyperparathyroidism is commonly found in patients with vitamin D deficiency. However, it has recently been found in patients with less severe vitamin D deficiency or insufficiency (serum 25-hydroxyvitamin D [25 OHD] < 50 mmol/L). Hyperparathyroidism also contributes to bone loss, the development of osteoporosis and increased risk of low trauma bone fractures. Other biochemical findings associated with vitamin D deficiency include hypocalcaemia, hypophosphataemia and raised alkaline phosphatase.

Calcium and vitamin D dietary supplements have been shown to correct vitamin D insufficiency, but it may take more than one year for bone to normalise. In 2002, The Scottish Intercollegiate Guidelines Network (SIGN) recommended that all elderly people in care homes routinely receive these supplements without being tested for vitamin D deficiency. Vitamin D deficiency is so common in institutionalised adults with intellectual disability that vitamin D supplements are recommended to all residents.

Severe and enduring mental illness is associated with poor nutrition and unhealthy lifestyles. Neuroleptic medication, anti-epileptic drugs, inadequate vitamin D intake, the application of sunscreen and limited or no solar exposure over a prolonged period make patients in high security psychiatric environments more...
vulnerable to deficiency states with adverse effects on bone. Further, young adults may not have achieved peak bone mass prior to admission. In March 2006, four out of five patients on routine annual physical examination by a general medical practitioner (GP)/forensic physician providing primary care services to a secure psychiatric hospital were found to have hypocalcaemia and deficient or insufficient vitamin D. Three of these patients had secondary hyperparathyroidism. None suffered from a gastrointestinal malabsorption disorder or renal disease.

GPs have been urged to adopt a proactive approach to the care of people with severe mental illness and provide a service to patients in institutions at least equivalent to those available in the community, where physical health is a key component of the new GP contract. In the UK, GPs provide services to Ashworth, Broadmoor and Rampton high security hospitals as well as lower security settings. However, the very nature of patients’ mental disorders, challenging behaviours, learning disabilities and inability to give informed consent present practical problems to GPs working in secure environments.

The primary aim of this study was to determine the feasibility of screening for and treating vitamin D deficiency in forensic psychiatric patients in a high security environment. A secondary aim of the study was to estimate the prevalence of vitamin D deficiency and the associated risk factors within the entire patient population.

2. Method

2.1. Setting

The State Hospital (TSH) is a special security psychiatric hospital for men in Carstairs, South Lanarkshire, Scotland, at latitude 55 42 N. Routine primary healthcare is provided by GPs through regular surgeries, annual health reviews and chronic disease management.

2.2. Population

The study population comprised 157 male patients. An analysis of the hospital population reported that 69% had a diagnosis of schizophrenia, 55% a history of chronic physical disorder, 17% suffered from epilepsy and 89% were on neuroleptic medication.

2.3. Design

The design was a cross-sectional study based on achieving a sample of 30 patients (approximately 20% of TSH population). Patients were eligible for inclusion if they were scheduled for their annual physical examination by the GP, the date of which coincides with their admission date. It was agreed by TSH Research Committee, that blood tests would be taken as part of this routine review to avoid additional discomfort to the patient.

Obtaining ethical approval from the NHS Research Ethics Committee (REC) was protracted. In 2006, this required resubmission of materials for people with learning disabilities and additional resources to enable them to understand the information.

The first approach about the study was by letter to patients’ Responsible Medical Officers (RMOs) to confirm patients’ capacity to give informed consent. Thus patients were excluded from the study if, in the opinion of their RMO, they were too unwell, dangerous or violent. In 2007, around 8 of a sample of 30 patients were excluded because they lacked the capacity to consent. There was therefore a risk that the most vulnerable would be excluded from the study, which would be biased if favour of patients, who were well, ambulant and able to access the grounds. A new application for the inclusion of patients unable to consent for themselves under section 5 of the Adults with Incapacity (Scotland) Act 2000 (AWI) was submitted to the NHS REC. The Act’s provisions allowed for a next of kin or legal representative to assent on the patient’s behalf to participation in the study.

In addition to RMOs, legal representatives were also entitled to exclude or withdraw patients at any time. Patients selected could also refuse or withdraw at any point in the study. Final approval was granted by NHS REC and the TSH Research Committee in March 2008.

The first approach to patients was by letter sent at the same time as the routine annual invitation for a blood test, which precedes their annual physical examination. Illustrated information designed to be understandable to people with learning disabilities supplemented written guidance and support from a designated health professional. As the study aimed to assess feasibility, particularly in terms of acceptability, patients were asked to consent to each individual element of the study:

1. Consent to give an additional 10 ml of blood for vitamin D re-measurement
2. Consent to complete a questionnaire eliciting data on lifestyle (diet, dietary supplements, smoking and exercise) and demographics (age, ethnicity, psychiatric diagnosis and symptoms, length of admission, medication and entitlement to grounds access)
3. Consent to allow access to their routinely held health records
4. Consent for the results of their blood tests to be reported to the RMO

2.4. 25 OHD assays

Venous blood samples were withdrawn during the first week of April 2008 and sent the same day to a local district general hospital for biochemical assay, which included calcium, phosphate, alkaline phosphate and parathyroid hormone (PTH) levels. The local reference range for PTH was 0.8–5.0 pmol/l. Hyperparathyroidism is considered to exist at levels >6 pmol/l. Measures for 25-hydroxycholecalciferol (25 OHD) for vitamin D deficiency were measured by a LC-MS/MS method in Glasgow Royal Infirmary. Individuals with serum levels of 25 OHD <25 nmol/l were termed deficient, 25–50 nmol/l insufficient and >50 nmol/l sufficient.

2.5. Outcome measures

The primary outcome measure for the study was the number of participants accepting the invitation to take part in all 4 elements of the study. The secondary outcomes were the number of samples positive for vitamin D deficiency or insufficiency and the number of patients who accepted treatment for vitamin D deficiency.

2.6. Statistical analysis

Participation rates are reported as percentages with exact 95% confidence intervals. Continuous variables are summarised as median and quartiles or mean and standard deviation (SD) and compared between patient groups using t-tests or Wilcoxon tests, as appropriate. Categorical variables are summarised as numbers and percentages within each category and compared between patient groups with exact Fisher tests. To assess the associations between each variable and vitamin D levels, p-values and $R^2$ statistics from univariate linear regression analyses are reported. In
addition, geometric mean vitamin D levels by categories of the predictor variables are shown; for continuous predictor variables, categories were formed by dichotomising at the median. As this is an exploratory study, p-values are not corrected for multiple testing and therefore have to be considered as descriptive measures. All analyses have been carried out using R version 2.9.1.

3. Results

3.1. Feasibility of screening

3.1.1. Achieved sample

Health centre administration selected 83 consecutive patients scheduled to undergo their annual physical examination in order to obtain a quota sample of 30 patients for the study. Of that sample 6/83 (7%) were excluded by the RMO or legal representative. Consent to all four components of the study was given by 41/83 (49%) patients. None gave consent to fewer than the four elements of consent. Of the 41 who provided consent, 5/83 (6%) refused at the time blood should be taken. For 2 patients, no or insufficient blood could be obtained; blood was lost for one patient. This means altogether that 36 patients were willing to participate, of whom 33 could actually be analysed (Fig. 1). The percentage of patients willing to participate (36 of 83) was 43% (95% confidence interval 33%–54%), the percentage of analysable patients (33 of 83) was 40% (30%–51%).

3.1.2. Characteristics of achieved sample

Summaries of the patient characteristics that were available for all patient groups are given in Table 1, separately for patients who were included in the study, patients who were selected but not included and patients who were not selected for the study.

The mean age of the study sample was 44.1 years (SD = 10.8, range 23–63 years), which was slightly, but not significantly higher than in the patients not included in the study sample (mean = 40.7, SD = 11.4, range 19–69 years). There was one non-Caucasian participant (Chinese ethnicity).

The most common diagnosis was schizophrenia (including paranoid schizophrenia). In the study sample, 23 (72%) had a primary diagnosis of schizophrenia and 2 (6%) schizoaffective disorder. There were several patients with dual diagnoses including non-organic, bipolar disorder, delusional and dissociative personality disorder. Three patients (9%) had learning difficulties. There were slight differences in the distribution of diagnoses between the three patient groups (p = 0.047). Patients with learning difficulties were underrepresented in participants compared to non-participants (9% vs. 13%).

In the study sample, the median length of stay was 7.8 years (range 0.9–41.0 years) compared to 5.5 years (0.3–31.8) in all non-participants. The four most extreme lengths of stay (36, 38, 39, 41 years) were in the study sample.

The percentage of patients treated with olanzapine was higher in the study sample (30% compared to 15% in the patients not included), whereas fewer patients were treated with clozapine (21% in participants, 37% in non-participants). Patients were not prescribed or taking vitamin D supplements.

Grounds access (without an escort) was available to 79% of patients in the study sample and non-participants alike. In the selected patients, all who had grounds access used it (with or without an escort). In the non selected patients there was one patient with grounds access who did not use it. The duration and intensity of exposure to sunlight was not known.

3.2. Vitamin D deficiency

3.2.1. Detected prevalence

Table 2 summarises the characteristics of the 33 patients for whom vitamin D values were available, overall and separately for patients whose vitamin D levels were deficient (N = 19, 58%), insufficient (N = 11, 36%) or normal (N = 2, 6%). All 7 patients who had no grounds access were found to be vitamin D deficient. Three patients with vitamin D deficiency (16%) had biochemical evidence of secondary hyperparathyroidism (PTH >6 pmol/l).

![Flow diagram](image-url)
Table 1: Description of all patient populations, with p-values comparing participants with all non-participants. Summaries shown are median (inter-quartile range) for continuous variables, or N(%) for categorical variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Selected patients</th>
<th>Non selected</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>33</td>
<td>50</td>
<td>74</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47 (34, 50)</td>
<td>42 (34, 48)</td>
<td>40 (29, 49)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>23 (72%)</td>
<td>32 (65%)</td>
<td>49 (70%)</td>
</tr>
<tr>
<td>Mild learning disability</td>
<td>2 (6%)</td>
<td>7 (14%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Moderate learning disability</td>
<td>1 (3%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Unspecified non-organic psychosis</td>
<td>1 (3%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Delusional disorder</td>
<td>1 (3%)</td>
<td>2 (4%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Dissocial personality disorder</td>
<td>1 (3%)</td>
<td>1 (2%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Bipolar affective disorder</td>
<td>1 (3%)</td>
<td>1 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>5 (10%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Length of stay (years)$^b$</td>
<td>7.8 (2.0, 12.0)</td>
<td>6.3 (3.6, 12.7)</td>
<td>5.0 (1.8, 9.6)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>7 (21%)</td>
<td>15 (30%)</td>
<td>31 (42%)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>10 (30%)</td>
<td>7 (14%)</td>
<td>11 (15%)</td>
</tr>
<tr>
<td>Risperidone</td>
<td>3 (9%)</td>
<td>5 (10%)</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>Lithium</td>
<td>4 (12%)</td>
<td>5 (10%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>2 (6%)</td>
<td>2 (4%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Grounds access</td>
<td>26 (79%)</td>
<td>36 (72%)</td>
<td>62 (84%)</td>
</tr>
<tr>
<td>Grounds access used</td>
<td>26 (79%)</td>
<td>36 (72%)</td>
<td>61 (82%)</td>
</tr>
</tbody>
</table>

$^*$F-test, $^W$Wilcoxon test, $^#$Exact Fisher test, $^a$Not available for 6 patients, $^b$Not available for 3 patients.

Table 3 summarises the univariate association between vitamin D as a continuous variable (log-transformed) and several patient characteristics in linear regression analyses. The strongest association was found for grounds access ($p = 0.010$, $R^2 = 19.5$%), with a geometric mean vitamin D level of 24.2 nmol/l in patients with grounds access compared to 14.7 nmol/l in patients without grounds access. The second most strongly associated variable of those considered was PTH, for which the $p$-value was 0.097 and the $R^2$ value was 19.5%, with 36% had insufficiency (25 nmol/l) and 36% had insufficiency (25–50 nmol/l). The only variables for which relevant differences were found between the patients who participated and those who did not (for whatever reason) were the diagnosis and treatment with olanzapine. The feasibility of obtaining a representative sample with individual consent for research from TSH population is questionable, but although the study methodology did not focus on obtaining a representative sample, but a sample based on the annual review date, the sample is not too different from the whole population.

Nevertheless, even if the sample is not entirely representative, the results are still alarming, with only two patients presenting vitamin D levels in the normal range and more than half of the sample being vitamin D deficient. Whilst we could not demonstrate that either of the factors found to be different between those who participated and those who did not is associated with vitamin D deficiency, these differences suggest that the patients who did not participate might be more unwell than those who did. There was also a slight, if not significant difference in the proportion of patients who had grounds access, with less grounds access for those who did not participate, which could also be a reflection of their current health state. It may therefore be reasonable to assume that, if anything, the non-participants are more likely to be vitamin D deficient than the patients who participated. Therefore the estimated prevalence of vitamin D deficiency and insufficiency may have been underestimated. Given these results, it seems necessary to investigate possible interventions to tackle vitamin D deficiency in this patient group (and their acceptance), especially in patients who have no grounds access.

4. Discussion

4.1. Summary

This paper describes the first reported feasibility study of screening for vitamin D deficiency in a high security psychiatric environment in the UK. Overwhelming evidence of vitamin D deficiency is demonstrated in individuals with mental disorder involuntarily detained in TSH, where 58% of patients had severe deficiency (<25 nmol/l) and 36% had insufficiency (25–50 nmol/l). The only variables for which relevant differences were found between the patients who participated and those who did not was the diagnosis and treatment with olanzapine. The feasibility of obtaining a representative sample with individual consent for research from TSH population is questionable, but although the study methodology did not focus on obtaining a representative sample, but a sample based on the annual review date, the sample is not too different from the whole population.

4.2. Strengths

The study involved a significant proportion (20%) of the hospital population, which was representative in terms of age and
diagnosis, but not length of stay. The investigation withstood the scrutiny of a lengthy research ethics process.

4.3. Limitations

Exclusions were necessary as patients in TSH are detained ‘in order to protect any other person from serious harm’. Individuals excluded or withdrawing were also likely to have been more unstable at the time of the study than participants and consequently physically unwell. Patients have also repeatedly refused annual physical reviews. A large proportion voluntarily failed to respond or declined the invitation to participate in the study. Low educational attainment and learning disability, two potential barriers to participation, were addressed in the methodology.

It is therefore possible that the true prevalence of vitamin D deficiency in the hospital is higher than the estimated figures. Compounding this effect are reports that biochemistry may underestimate vitamin D deficiency in 20% of affected cases. Blood samples were taken during the first week in April, when vitamin D levels were likely to be at their lowest. Owing to the decision to inform and treat affected individuals promptly, there was no opportunity to retest the cohort at the end of the summer, when vitamin D levels are expected to be highest. Given the weather and restrictions to movement within the hospital at the time of the study, in reality, the disparity may not be significantly different.

4.4. Feasibility

A recent prevalence study identified vitamin D deficiency in a small sample of male inpatients undergoing rehabilitation in a low security psychiatric service. The authors do not address the issue of the capacity to give consent. Under AWI legislation, research participants must be capable of making, communicating, understanding and retaining memory of the decision to consent. Otherwise, in order to obtain consent, it is necessary to implement section 5 of the AWI legal framework, whereby a legal representative can assent to participation. While not a weakness in the TSH study, legal restriction indicates the limited feasibility of conducting such research in a secure environment.

Owen et al assessed mental capacity to make decisions on treatment by diagnosis and legal status in adult acute psychiatric inpatient units at the Maudsley Hospital, London. Using the
MacArthur competence assessment tool for treatment, the prevalence of mental incapacity in patients with schizophrenia was 81% and, when the patient was involuntarily detained, 86%. When the prevalence of mental incapacity in patients with schizophrenia was 4.5. Vitamin D deﬁciency may have symptomatic osteomalacia. He adds that secondary hyperparathyroidism accelerates osteopenia and osteoporosis.27,28 Osteoporosis is also an adverse effect of anti-epileptic medication such as sodium valproate used as a mood stabiliser.29 It would then seem reasonable to assess fracture risk, but the mean age of this sample was young: 43 years (range 23–62 years). Discussion with the local rheumatologist has resulted in only those patients over 40 years with vitamin D deﬁciency and secondary hyperparathyroidism undergoing dual-emission X-ray absorptiometry (DXA) scans to measure bone mineral density.

The association between mental illness and poor physical health was reported in 193430 two years before building work began at TSH. Much physical ill health remains undetected.31 Several initiatives funded by government departments have attempted to tackle the issue in the community.15,32 Structured screening programmes are recommended for long stay psychiatric patients.31 An initiative for GPs working in secure psychiatric units has been launched by the Royal College of General Practitioners Doctors Working in Secure Environments Group, which aims to address the social exclusion issues in relation to general practice services and the provision of care to patients in secure environments.34

4.6. Diet

Research has examined diet in prisons35,36 and the potential to link prison dietary standards to behaviour. No calcium or vitamin D is currently added to patients’ diets in TSH, but importantly for patients’ management in TSH, hypovitaminosis D is thought to aggravate depression, psychoses, convulsions and epilepsy.37 However as over 90% of vitamin D is derived from solar exposure, even a healthy and well balanced diet containing oily ﬁsh, eggs and margarine is unlikely to provide patients with the vitamin D they need.

4.7. Vitamin supplementation

Concerns about the increased risk of death from cardiovascular disease associated with vitamin D deﬁciency38 were compounded by a meta-analysis by Bolland, which reported a moderate increase in the risk of myocardial infarction in women taking calcium supplements, which are commonly used in combination with vitamin D.39 TSH’s exclusively male population, over 70% of which has a diagnosis of schizophrenia is already at greater risk from cardiovascular disease from lifestyle factors and diabetogenic medication.40 In June 2008, 83% of patients in TSH were overweight or obese (BMI > 25) and 13% were diabetic, although smoking prevalence is decreasing following smoking ban legislation.

Multivitamins containing vitamin D may be considered a pragmatic solution to nutritional deﬁciency, but the pharmacological risks associated with these unlicensed medicines are not known.

At the end of the study, on 1st April 2009, of the initial sample, 15/31 of eligible patients had accepted and continued supplements giving a maximum daily dose of 194 mg (4.8 mmol) calcium. Bolland’s supplementation review included studies with calcium doses greater than or equal to 500 mg/day.

While there would appear to be a robust ethical argument in favour of vitamin D supplementation, evidence from large interventional (observational or randomised) studies of vitamin D supplementation is reported to be lacking.41 Treatment with vitamin D alone has been delayed because of a lack of suitable licensed products of consistent strengths, presentations and quality. The Medicines and Healthcare Products Regulatory Authority.
exposure, application of UV guidance and policy. Effective use of grounds access, safe sunlight secure environments requires careful consideration and national policy makers. The logistical and financial implication of grounds access to secure environments requires careful consideration and national guidance and policy. Effective use of grounds access, safe sunlight exposure, application of UV filters and wearing of appropriate clothing are areas for development in a patient education programme. Patients are already encouraged to make healthy choices from a menu that includes vitamin D rich foods such as eggs and oily fish. However, health promotion programmes in TSH acknowledge the link between boredom, powerlessness, lack of hope and limited opportunities for health improvement, which has a major impact on the health of this vulnerable population. These factors support systematic screening for vitamin D deficiency on admission and at annual health reviews and routine supplementation, where patients are deprived of solar exposure. Patients should, wherever possible, make informed decisions having been informed of treatment options, risks and benefits before commencing medication. It remains an ethical challenge how to manage the most vulnerable patients at greatest risk of vitamin D deficiency and who lack the capacity to give informed consent to screening, supplementation and monitoring.

5. Conclusion

Significant and serious vitamin D deficiency has been confirmed in forensic inpatients in a secure psychiatric hospital. Systematic screening is necessary due to mental health and consent issues. Consideration should be given to vitamin D enriched diets, supplementation and access to adequate sunlight. This study is relevant to other secure environments including Ashworth, Broadmoor and Rampton high secure hospitals in the UK, prisons, the RCGP Doctors Working in Secure Environments Group and national policy makers.

Conflict of interest

All authors state they have nothing to declare.

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Ethical approval

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