to diagnose and treat empirically disorders such as fibromyalgia, polymyalgia rheumatica, or chronic fatigue syndrome without knowledge of a patient's vitamin D status.

Sattar and colleagues also question the need to measure 25-hydroxyvitamin D in patients with osteoporosis, contending that medication with tablets containing calcium and vitamin D will cover all eventualities. However, the UK's National Institute for Health and Clinical Excellence sensibly recommends vitamin D supplementation only for patients who are not already vitamin D replete.[2] Further, dual-energy X-ray absorptiometry cannot distinguish low bone density resulting from osteoporosis from that of osteomalacia, so failure to request 25-hydroxyvitamin D measurement will necessarily lead to inappropriate treatments. Recent guidance highlights the inadequacy of commonly used calcium and vitamin D products that contain just 400 IU of the vitamin for treating patients with profoundly low concentrations of 25-hydroxyvitamin D in serum. Such patients require higher pharmacological doses.[3,4]

Although the current situation is far from ideal, we feel that Sattar and colleagues overlook several situations in which quantification of 25-hydroxyvitamin D is important, and cast unwarranted aspersions on the ability of primary-care physicians to make clinically based requests in this area.

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Naveed Sattar and colleagues[1] highlight increasing requests for vitamin D measurement and the associated costs. The need to contain health-care costs is universal, especially in western countries where they are increasing at an unsustainable rate. We agree that vitamin D deficiency is prolific worldwide. However, we have major areas of disagreement regarding testing and monitoring of vitamin D.

There are many correlates with serum 25-hydroxyvitamin D concentrations, but studies that used common laboratory tests and included latitude and seasonality were unable to predict vitamin D deficiency, suggesting that there is no substitute for 25-hydroxyvitamin D testing.[2] We too have noticed a marked increase in testing for vitamin D status in recent years. However, in a study of six Veterans Medical Centers in the southeastern USA, the lowest overall medical costs were in the medical centres that did follow-up vitamin D testing.[3] In particular, across all sites, vitamin D deficiency combined with lack of monitoring predicted increased inpatient health-care costs.[3]

One option to reduce the costs of vitamin D testing would be to supplement the general population with 1000–2000 IU vitamin D3, as recommended by the Endocrine Society.[4] Indeed, such an approach has been postulated to result in a substantial reduction in global health-care costs.[5] The greatest benefits accrue to those with serum 25-hydroxyvitamin D concentrations below 50 nmol/L; optimum concentrations should be at least 75–100 nmol/L.[4,5]

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Authors' reply

We welcome further debate on the issue of vitamin D testing, and, given the range of responses received, there is clearly a need for it. Andrew Grey and colleagues provide interesting data to suggest that vitamin D requests are dominated by a relatively small proportion of clinicians. Our hospital biochemistry department in Glasgow, UK, recently applied selected restrictions on requests for 25-hydroxyvitamin D testing and is seeing similar efficiencies. Thus we agree that, if the evidence base is ignored, direct measures to limit health-care expenditure on inappropriate vitamin D tests are warranted.

We agree with Pascal Caillet and Anne-Marie Schott that non-standardised assays are a barrier to

the incorporation of accurate and reliable 25-hydroxyvitamin D testing and that misclassification remains a challenge. That noted, whether even robust measurement of the 25-hydroxyvitamin D metabolite in serum accurately reflects whole-body vitamin D status in all individuals remains uncertain.

Stewart Pattman and colleagues suggest that fibromyalgia and chronic fatigue are appropriate conditions to request vitamin D measures. We cannot identify convincing evidence to support this assertion, and there is no evidence from large placebo-controlled randomised trials:[1] replete vitamin D status does not exclude these disorders, and there is no robust evidence that vitamin D supplementation improves symptoms. Further, people with fatigue and pain will probably spend less time outdoors, which leads to lower 25-hydroxyvitamin D (ie, reverse causality).

We agree that diagnosis of osteomalacia requires biochemical testing that could include 25-hydroxyvitamin D. We do not, however, believe that an increasing incidence of osteomalacia accounts for the increasing vitamin D requests. The National Institute for Health and Clinical Excellence guidelines for the secondary prevention of osteoporotic fragility fractures in postmenopausal women state that "vitamin D supplementation should be provided unless clinicians are confident that women who receive treatment for osteoporosis…are vitamin D replete".[2] Given that a significant majority of elderly women, particularly in northern latitudes, and particularly through the winter months, are likely to have insufficient 25-hydroxyvitamin D, the benefit of widespread testing is unclear, especially if supplements are to be prescribed irrespective of the result.

Our comments were intended as general guidance and clinical decisions are best made on a case-specific basis with specialist input as appropriate. Furthermore, we respectfully suggest that asking clinicians to think through critically whether vitamin D testing is appropriate, particularly among asymptomatic people and particularly in conditions not linked to bone disease, is not to cast "unwarranted aspersions".

Alan Peiris and colleagues suggest that latitude and seasonality cannot predict vitamin D deficiency, citing data from an observational study of individuals who attended a vitamin D seminar and took supplements. Latitude and season are not investigated in that paper.[3] Peiris and colleagues suggest that widespread supplementation programmes could proceed without further evidence or trials of efficacy or safety. The Institute of Medicine does not seem to concur with this view.[4] We therefore reiterate the need to resist making causal inferences on the basis of observational evidence, which Peiris and colleagues seem to advocate.[5]

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Bedside detection of awareness in the vegetative state


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Damian Cruse and colleagues (Dec 17, p 2088)[1] report EEG evidence of command-following in three patients apparently in the vegetative state. However, the known alterations of brain function after severe injury associated with vegetative state and minimally conscious state, along with the relatively weak EEG signals seen in the study's healthy controls, raise concerns about the validity of the findings.

Previous studies that used EEG signals to identify motor imagery in paralysed conscious patients[2,3] or to indicate awareness in disorders of consciousness[4] used simple EEG features: systematic changes in voltage ("power") in alternating imagery and rest conditions. Cruse and colleagues instead use a classifier based on a combination of many EEG parameters. Neither raw EEG, nor individual parameter values, nor their weightings by the classifier are presented. Thus, it is difficult to assess the approach's biological underpinnings, and credibility hinges on rigorous statistical controls.

However, establishment of such controls is daunting: the EEG is statistically non-stationary and typically contains gradually changing contaminants such as electromyographic noise (including the known stimulus-linked startle in patients in the vegetative state[5]). In a block-design study, it is therefore difficult to separate selective task-driven responses from artifactual changes that happen to covary with task. Cruse and colleagues' use of 0·5 s of pre-tone brain activity is an insufficient control. In comparison with the 3 s analysed post-tone, the pre-tone control classifier is likely to be insensitive to the confounds that must be excluded.