Table 1

<table>
<thead>
<tr>
<th></th>
<th>Primary care</th>
<th>Secondary care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of prescriptions reviewed of subjects taking bisphosphonate drugs</td>
<td>368</td>
<td>164</td>
</tr>
<tr>
<td>Percentage with prescription for vitamin D supplements</td>
<td>44%</td>
<td>32%</td>
</tr>
<tr>
<td>Number of samples obtained for vitamin D measurement</td>
<td>93</td>
<td>98</td>
</tr>
<tr>
<td>Age of subjects (yr): mean (range)</td>
<td>71 (24–90)</td>
<td>73 (38–92)</td>
</tr>
<tr>
<td>Female (n)</td>
<td>82</td>
<td>63</td>
</tr>
<tr>
<td>Subjects taking corticosteroids: n (%)</td>
<td>21 (23%)</td>
<td>75 (77%)</td>
</tr>
<tr>
<td>Vitamin D &lt;30 nmol/l (insufficiency): n</td>
<td>25</td>
<td>37</td>
</tr>
<tr>
<td>Number (%) of subjects with deficiency/insufficiency</td>
<td>49 (53%)</td>
<td>77 (79%)</td>
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</table>

Overall 40% of subjects were receiving vitamin D supplements, in all cases as a combined calcium and vitamin D formulation (Table 1). Subjects recruited from primary care were more likely to receive a coprescription for vitamin D, even though subjects recruited from secondary care were older, had more comorbidity, and had higher rates of vitamin D deficiency and insufficiency. A small number of subjects were taking self-prescribed multivitamin or cod liver oil supplements. These subjects were included in the sample and their results did not differ from those for the overall sample. Subjects recruited in secondary care were more likely to have had their initial prescription for bisphosphonate medication from a hospital specialist rather than their general practitioner. In 40% of cases bisphosphonates were being given for the prevention or treatment of steroid-related osteoporosis. Steroid use was more frequent in the secondary care sample. There was no correlation between age and vitamin D levels; four patients from the primary care sample, aged under 50 yr, had vitamin D deficiency and one had insufficiency. Females had non-significantly lower levels of vitamin D.

These results demonstrate that there are low levels of coprescription of vitamin D with bisphosphonates among both hospital and non-hospital attendees, and high rates of vitamin D deficiency in those that are not supplemented. On the basis of these results we advocate the widespread coprescription of vitamin D supplements when bisphosphonate drugs are used for the prevention or treatment of osteoporosis. During the study all subjects recruited in secondary care, who were not taking a vitamin D supplement prior to the study, were started on a combined calcium and vitamin D supplement once their blood sample was taken, as it is our policy to coprescribe calcium and vitamin D supplements with bisphosphonate medication. The results of the study have been fed back to participating general practices but we do not know what proportion of the subjects recruited in primary care have subsequently been started on supplements. Although calcium intake was not addressed in this study, many of these patients also require calcium supplementation, so a combined supplement is probably the easiest way of achieving this.
withhold or discontinue AZA/MTX had been made at consultant level, despite previous reports that transaminase elevations may be found in myositis [2–4] and other muscle diseases [4–6]. Transaminases are important intracellular components of metabolic function in many cells, including those of muscle, and elevated ALT levels may reflect transaminase leakage into the bloodstream, due to myofibrillar damage, in a manner analogous to lactate dehydrogenase and creatine phosphokinase (CPK) leakage [7]. The purpose of this ethically approved study was to examine the relationship between serum ALT and CPK levels in myositis patients, in order to establish whether ALT levels could be predicted from CPK levels.

From the Salford adult-onset myositis (disease onset after 18 yr of age) database, 61 patients were identified with probable or definite myositis, according to Bohan and Peter criteria [8, 9]. Of these patients, 18 had DM, 22 PM and 21 PM as part of a connective tissue disease overlap. In a retrospective analysis of these 61 patients' data, 208 occasions were identified when their ALT, CPK and alkaline phosphatase (ALP) levels were measured together in the same laboratory, and where all the results were available. As this study was retrospective, the results of other hepatic transaminases or γ-glutamyl transferase were not available, so ALP was used instead as a surrogate ‘other’ marker of hepatic function. Correlations between the log-converted values of ALT, CPK and ALP were made using linear regression analysis, and scatter-graph plots were constructed. The results demonstrated a strong correlation between serum CPK and ALT (r coefficient = 0.78, R² = 0.59, P < 0.0001; Fig. 1), but no correlations between ALT and CPK (r = 0.04, P = 0.7), or between ALP and CPK (r = −0.1, P = 0.5). An equation of the line can be derived from the Fig. 1, describing the correlation between log CPK/ALT values [logCPK = 1.47 × (logALT + 0.18)], and allows prediction of ALT levels from measured CPK levels. For instance, a myositis-induced CPK rise to double the upper normal limit, i.e. to 390 U/l (log value 2.59), would be associated with an ALT level still just within the laboratory normal upper limit, of 50 U/l (log value 1.7), while a myositis-induced ALT rise to 100 U/l would not be expected until CPK levels had risen to around 1000 U/l.

That not all rheumatologists appreciate that ALT rises occur in active myositis was the stimulus for this brief study. The knowledge that CPK and ALT correlate so well and that ALT levels can be predicted from CPK levels should reassure those treating myositis patients that ALT elevations are probably of muscle origin, and remind that elevated ALT values do not necessarily require exhaustive or invasive investigations. As ALP does not rise despite obvious ALT rises should further reassure. If, following the initiation of corticosteroids in new-onset disease, CPK and ALT levels remain elevated but their log values correlate in a fashion similar to that seen in the Fig. 1, and ALP is normal, then it appears safe to add AZA/MTX if required. Similarly, during disease relapses requiring AZA/MTX dose increments, these appear safe if the log CPK/ALT values clearly correlate and ALP remains normal. Rigorous monitoring would, of course, still be required. Three of the tertiary patients stimulating this study were from hospitals routinely measuring transaminases other than ALT, e.g. aspartate aminotransaminase (AST). A formal correlation between AST and CPK was not possible due to the small patient numbers and the fact that AST had been measured in three laboratories, but high AST levels were also noted when CPK levels were high, in keeping with previous reports [3, 4]. If transaminase levels do not fall as CPK levels fall with treatment, or if ALT levels are inappropriately high for the measured CPK in stable disease, investigations of hepatic function should then be prompted.

The authors have declared no conflicts of interest.

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The RAGE G82S polymorphism is not associated with rheumatoid arthritis independently of HLA-DRB1*0401

Sir, The receptor for advanced glycation end-products (RAGE) has been shown to play a role in several pathologies,