In both the ICD10 and DSM IV definitions of depression, pain is briefly mentioned as a possible symptom but is certainly not considered as a defining symptom such as low mood or as a somatic symptom. This is surprising since pain symptoms and depression commonly coexist, as has been demonstrated in a number of studies (see Table 1). Not only does there appear to be a clear association between pain and depression, but furthermore, there is a recognised concern that the presence of pain often negatively affects the recognition and treatment of depression: depressed patients have been shown to be far more likely to present with pain symptoms than they are to present with affective symptoms and it has been estimated that if all patients from general practice who presented with painful conditions were evaluated for possible depression, then 60% of previously undetected depressive cases would have been recognised. Furthermore, when depression is recognised to be present in conjunction with pain, clinicians are more likely to focus on treating the pain and are less likely to consider psychological treatments, leading to worse outcomes.

The situation is further complicated by the fact that the subjective experience of pain is likely to have cognitive, emotional and behavioural components in addition to the underlying biological component and, in some cases, there may be no underlying biological component at all. It is likely to be very difficult to distinguish between these components, but for the purposes of considering the effect of pain on depression, the origin of the pain probably makes little difference to the established association.

When pain and depression are recognised and the clinician does focus on treating the depression, the presence of pain appears to increase the resistance of depression to treatment (see Table 2 in the online version of this article). As might well be expected, a combined diagnosis of both pain and depression accounts for a far greater healthcare resource utilisation in both primary and secondary care, since patients with both pain and depression have an increased number of GP visits, an increased rate of investigations, a higher rate of antidepressant drug switching and increased referral to secondary care. The combination of both pain and depression also has an additive effect on the work days lost through both sickness absence and productivity.

**Aim**
We looked to identify if there were any combined pain and depression tools by using a comprehensive literature search. We examined our search results to help outline and propose a future mechanism of screening for comorbidity of depression and pain in a primary care setting.

**Method**
We conducted an extensive literature search to investigate if any screening tools simultaneously could screen patients for both depression and pain. This was undertaken with a systematic MEDLINE, EMBASE and AMED search over the years 1946–2015 using the combined terms ‘pain’ AND ‘depression’ combined with the individual terms ‘screening’, ‘checklist’, ‘tool’, ‘questionnaire’, ‘inventory’ or ‘scale’.

**Results**
From our literature search, we found a total of 43 articles but none offered a combined general screening tool for depression and pain. The articles were analysed and divided into relevant subsections. The majority focussed on eliciting an altered mental state in conditions with known chronic pain. Two articles, however, did assess for both depression and pain: Tamiya et al. looked at pain, anxiety and depression in 145 Japanese women with rheumatoid arthritis. They used visual analogue scales to measure depression and anxiety and compared these with standard
measures and to a pain analogue scale. However, their study was restricted to patients with rheumatoid arthritis, a long-term condition where pain is central to the presentation, and was not replicated in other populations of chronic conditions. Furthermore, the sample population was selective and the tools used as diagnostic as opposed to screening. Luppi et al. looked at pain, anxiety and depression in 81 patients with leukaemia and 118 patients with solid cancers. They used a Likert scale (0–10) for pain, depression and anxiety and compared these with standard measures for depression and anxiety. However, again their study was restricted to patients with a specific condition – malignancy – and was not replicated in other chronic conditions.

We also found a further similar study, not from within our search criteria, which employed a visual analogue scale to elicit anxiety, depression and catastrophising in 45 patients with neck pain. Again, as with Tamiya et al., the study was restricted to a single presentation of pain, used small numbers and crucially was not tested as a screening tool.

In summary, our search did not reveal any validated tool which could be used to screen for comorbid pain and clinical depression in primary care. In the absence of such a combined tool, we then considered common screening tools in use for depression and pain separately.

There are a number of well recognised screening tools for depression. In the general practice setting, three tools are recommended in the Quality and Outcomes Framework (QOF) guidance for the evaluation of depression. Furthermore, for patients with a
The neurobiological hypothesis of the coexistence of pain and depression

Physical pain can be considered to be a combination of the sensory component of the pain and the associated affective component of the pain. Although psychological pain, such as psychological distress, does not involve a painful stimulus, it still signals a threat to the body in the same way as physical pain and thus the neural mechanisms, including the hypothalamic-pituitary axis, are still activated as part of the stress response. It has been shown that the nociceptive pathway for psychological pain is in fact similar to the pathway involved in the processing of the affective component of physical pain. Through this mechanism, it is hardly surprising therefore that pain and depression are associated.

More specifically, the association can be considered in terms of commonality of neurotransmitters. It has long been accepted that, biochemically, depression can be attributed to a deficiency in serotonin, noradrenaline and dopamine. There is now increasing understanding of the descending system of pain modulation whereby the periaqueductal grey acts as a relay between forebrain and midbrain structures and the brainstem. Within this relay are serotonergic and noradrenergic neurons which dampen pain signals transmitted from the periphery by depressing the activity of nociceptive neurons in the spinal dorsal horn. This system serves to determine our affect and attention to stimuli and usually modulates this so we are able to focus more on external stimuli rather than those from within the body. However, in the scenario of a deficiency of serotonin and noradrenaline, this system likely loses its modulatory effect such that in depression, multiple pain symptoms are experienced and the presence of pain leads to increased focus on the pain and a lowered affect. This hypothesis has been demonstrated experimentally in a recent study comparing patients with chronic pain in fibromyalgia with and without depression, which showed that inhibition of pain (via the diffuse noxious inhibitory controls [DNIC]) is further reduced in comorbid depression.

Recent studies have highlighted that the central nervous system undergoes long-term plasticity in the presence of chronic pain and depression. The underlying neural circuitry and molecular signalling pathways that underlie this are beginning to be understood. The molecular signalling pathways include not only the neuropeptides serotonin, noradrenaline and dopamine as described above, but also include a role for glutamate signalling, neurotrophic factors (e.g. brain-derived neurotrophic factor [BDNF]) and neuromodulatory lipids (e.g. endocannabinoids). It seems likely that these complex changes, which result from chronic pain and depression together, are at the root of why chronic pain and depression together are so difficult to treat; but further work is needed in this area.

Treating the problem

If pain and depression share common deficiencies in neurotransmitters, then it seems logical to suggest...
that antidepressant therapy, which boosts these neurotransmitters, could be used in the treatment of pain. To this end, it has long been recognised that tricyclic antidepressants have a role in treating chronic pain. More recently, an evidence-based review of using antidepressants in chronic pain showed that serotonergic-noradrenergic antidepressants appear to be more effective than serotonergic antidepressants. One specific serotonergic-noradrenergic antidepressant that is becoming increasingly popular is duloxetine. The effectiveness of duloxetine in treating chronic pain was reviewed recently in a 2014 Cochrane review, which focussed on the use of this medication in treating painful neuropathy, chronic pain and fibromyalgia. The authors concluded that there was a significant improvement in pain in all three types of condition, but with the evidence being strongest in diabetic neuropathy. It is of particular interest that of all the different types of pain, it is neuropathic pain, rather than acute or inflammatory pain, that is most successfully treated with antidepressants. Using a model of neuropathic pain employing peripheral nerve injury, it has been shown in rodents that this type of pain can induce depressive-type symptoms, including anhedonia and behavioural despair.

Of course, in patients presenting with chronic pain and depression, an antidepressant is not the only solution. Many of the cognitive, behavioural and affective factors that are critical in the development of depression are also relevant to the development of chronic pain, which helps to further explain their association. Hence, a patient with both depression and pain needs a multidisciplinary approach to the problem from psychiatrists, psychologists and pain specialists with an understanding, empathetic style and inclusion of education for patients and their families about how the two conditions are likely to be linked. There is a wealth of evidence to suggest that non-pharmacological interventions such as cognitive behavioural therapy, behavioural therapy and acceptance-based therapy have some effect in treating chronic pain and improving mood outcomes. More recent work has demonstrated functional neuroimaging changes in chronic pain patients (in the Default Mode Network) which can be altered by these interventions and correlate with clinical outcomes.

**Addressing the problem: the need for a new screening tool**

Whilst it is encouraging that we are beginning to understand the association between depression and

![Figure 1. Recommended approach for pain and depression screening for patients with long-term physical health conditions presenting to the general practitioner](www.progressnp.com)
pain, the likely mechanisms involved and possible treatment options, it is of little help to the typical patient if the coexistence of the two conditions is frequently missed. Instead, what is really needed is a simple-to-use screening tool for any patient presenting to a general practitioner with either pain or depression alone, to assess if the two coexist. In the cases where coexistence is demonstrated, the patient can then be treated appropriately with consideration of both problems simultaneously.

The fact that such a screening tool does not exist is surprising since untreated depression may adversely affect ability to treat pain and disease-specific outcomes. Therefore, the argument for including pain screening when assessing patients with long-term conditions for depression is strong.24

Work is clearly needed to develop and validate a combined screening tool for both pain and depression for use with patients suffering from long-term physical health conditions. Here we consider the patient presenting to primary care with a long-term physical health condition. There are separate screening tools that could be used to investigate the presence of either depression or pain alone but we suggest that using an integrated, combined tool will ensure consistency in the primary care approach to long-term health conditions. Our choice of a suitable integrated tool must also consider the time pressures within general practice where it would not be practical to use a combined version of two lengthy screening tools. To this end, we note that since NICE recommends that patients with such conditions are all screened for depression, by asking two standard screening questions, we feel that the simplest and least time-consuming option to incorporate pain screening for these patients is to add a third screening question about pain. The NICE guidelines further recommend that if either question regarding depression screens positive, then further questions are asked to clarify the situation. We therefore recommend that an additional two questions could be added for those who screen positive for pain, which ask about the nature and the severity of the pain. With consideration of the various pain scales and of the time constraints within general practice, we feel that the best option is to use the numerical rating scale (0–10) as the means to assess the pain severity. Our recommended approach is illustrated in Figure 1, the findings of which could be recorded electronically within the patient notes. We suggest that including pain screening as part of depression screening in patients with long-term physical health conditions will ensure that any potential pain component is not overlooked. This thereby ensures that in the cases of any identified depression complicated by the presence of pain, the treatment of this pain is incorporated into the treatment of the depression and is therefore more likely to be successful.

We suggest that this simple screening tool could be used by a practice nurse as part of the annual review of any chronic illness. Should the three screening questions or the further questions used thereafter suggest the existence of newly identified chronic pain and/or depression, then the patient could be referred to the general practitioner for further discussion and treatment if necessary. In future work we plan to test the feasibility of this screening tool in correctly identifying new cases of pain and/or depression in chronic illness and later, the effect that this earlier identification can have on outcomes.

**Summary**

There is a strong association between pain and depression and the presence of pain negatively affects the recognition and treatment of depression. Their coexistence suggests a shared neurobiology. Early recognition and treatment of this comorbidity could have significant impact on patient outcomes and health service costs. Failure to do so could lead to treatment resistance, negative clinical and social impact and increased costs to health and social sectors. It is thus imperative that this comorbidity be recognised early to allow specialist treatment options to be considered, including the use of serotonin-noradrenergic antidepressants.

Sadly, at the present time, patients presenting with pain alone are not commonly screened for depression and conversely, patients presenting with depression alone are not commonly screened for the coexistence of pain. It is surprising that a single screening tool to assess patients with either condition for the coexistence of the other has not yet been developed. We believe that such a screening tool would lead to significantly better diagnosis, referral and hence treatment. We believe that we have presented the evidence to suggest an easy-to-use self-reported screening tool for patients presenting to their general practitioner with chronic illness to screen for both depression and pain. This could also be used in the context of patients presenting either with pain or depression to screen for the presence of both conditions.

*Tables 3, 4 and 5 are online only, available free to view on the Progress in Neurology and Psychiatry website: [http://www.progressnp.com](http://www.progressnp.com)*
Dr Cocksedge is CT3 in Psychiatry at Cornwall Partnership NHS Foundation Trust; Dr Shankar is a Consultant Neuropsychiatrist at Cornwall Partnership NHS Foundation Trust in Truro, and Honorary Associate Clinical Professor at Plymouth and Exeter Medical School, and Dr Simon is a GP at Bearwood Medical Centre in Bournemouth, Executive Editor – Innovate, and Editor, Oxford Handbook of General Practice.

Declaration of interests
No conflicts of interest were declared.

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<th>References</th>
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Table 3. The results of the literature search* to investigate if any screening tools simultaneously could screen patients for both depression and pain
(∗A MEDLINE search was done for articles combining the terms ‘pain’ AND ‘depression’ combined with the individual terms ‘screening’, ‘checklist’, ‘tool’, ‘questionnaire’, ‘inventory’ or ‘scale’. A total of 28 citations were found and are listed, subdivided into categories)
### Table 4.

Three tools used in the general practice setting to screen for depression, as recommended in the Quality and Outcomes Framework (QOF) guidance, and the NICE screening questions for depression in patients with chronic illness, compared with the recognised ‘gold standard’ in clinical research, the Hamilton Rating Scale for Depression

<table>
<thead>
<tr>
<th>Screening tool for depression</th>
<th>Type of screening tool</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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</table>
| Patient Health Questionnaire (PHQ-9; Kroenke et al. 2001)\(^7^8\) | Self-reported 9-item questionnaire which diagnoses depression and assesses severity; based on DSM-IV criteria | • Quick to use  
• Self-reported scale  
• Allows diagnosis of major depression and assessment of severity  
• Well validated and documented in a variety of populations | • Self-testing carries risk of patient adjusting their answers to fit their own agenda\(^7^9\)  
• Concerns regarding validity of determined severity\(^8^\) |
| Hospital Anxiety and Depression Scale (HADS; Zigmund et al. 1983) \(^8^0\) | Self-reported 14-item questionnaire; assesses both anxiety and depression; has been validated for use in primary care despite its name; assesses severity | • Quick to use  
• Self-reported scale  
• Allows diagnosis of depression and anxiety separately | • Self-testing carries risk of patient adjusting their answers to fit their own agenda\(^7^9\)  
• Concerns regarding validity of determined severity\(^8^\)  
• Exclusion of somatic items may represent a reduction in face validity\(^8^1\) |
| Beck Depression Inventory – Second Edition (BDI-II; Beck et al. 1996)\(^8^2\) | Self-reported 21-item questionnaire; diagnoses depression and assesses severity; based on DSM-IV criteria | • Quick to use  
• Self-reported scale  
• Allows diagnosis of major depression and assessment of severity  
• Includes some somatic symptoms  
• Well validated and documented in a variety of populations | • Self-testing carries risk of patient adjusting their answers to fit their own agenda\(^7^9\) |
| NICE guideline CG91 screening for depression in patients with a long-term physical health problem\(^7^\) | Two screening questions asked by GP to patient. If either positive then further questioning takes place | • Very quick to use  
• Specifically designed for patients with long-term physical health problems in the GP setting | • So brief and quick that symptoms may be missed, especially somatic symptoms |
| Hamilton Rating Scale for Depression (HRSD-17; Hamilton. 1960)\(^8^3\) | Clinician-rated 17-item questionnaire used for assessing the severity of depression | • As clinician-rated, less bias introduced by patient’s own agenda  
• Useful in assessing the effects of drug therapy | • Requires clinician to complete  
• Not intended as a diagnostic instrument |
<table>
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<tr>
<th>Pain rating scale</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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</table>
| Visual Analogue Scale (VAS; reviewed in Williamson, et al. 2005) | A self-reported scale. The patient marks their pain on a 100mm line ranging from 'no pain' to 'worst imaginable pain'. This is measured in mm, giving 101 levels in pain intensity. | • Quick and simple to use  
• Can be parametrically analysed  
• Shown to be the most reliable and valid when comparing VAS to VRS and NRS  
• Detects small changes in pain | • Only assesses pain severity  
• Must be administered on paper or electronically, so difficult to use in clinical practice  
• Patients with cognitive impairment less able to produce consistent scores |
| Numerical Rating Scale (NRS; reviewed in Williamson, et al. 2005) | A self-reported scale, using a 11 (0–10), 21 (0–20) or 101 (0–100) point scale with end points of 'no pain' versus 'the worst possible pain'; can be presented verbally or graphically. | • Quick and simple to use  
• Can be parametrically analysed  
• Detects small changes in pain | • Only assesses pain severity  
• Poor reproducibility has been demonstrated in one study, but lack of other studies to confirm this |
| Verbal Rating Scale (VRS; reviewed in Williamson, et al. 2005) | A self-reported scale involving a list of adjectives offered to describe pain intensity and then adjectives are assigned numbers. | • Quick and simple to use  
• Preferred by some patients due to simplicity | • Only assesses pain severity  
• Intervals between each rank number are not necessarily equal, leading to possible misinterpretation  
• Can only be analysed using non-parametric statistics  
• Insensitive to small changes in pain |
| Brief Pain Inventory – short form (Cleeland, et al. 1994) | A self-reported scale which includes a severity assessment like the NRS but scores pain in the last 24 hours ‘on average’, ‘at its worst’, ‘at its least’ and ‘right now’. The arithmetic mean of the four severity items can be used as measures of pain severity. Also assesses location of pain, analgesic usage and impact of pain on daily function. | • Explores the pain in more detail than just a severity scale  
• High test-retest reliability  
• Widely used in clinical research | • Takes longer to complete than those above  
• Unsuitable for patients with cognitive impairment |

Table 5. Examples of common generalised pain scales in use which could be used in a primary care setting.