ABSTRACT
Chronic pain is an important clinical problem affecting significant numbers of children and their families. The severity and impact of chronic pain on everyday function is shaped by the complex interaction of biological, psychological and social factors that determine the experience of pain for each individual, rather than a straightforward reflection of the severity of disease or extent of tissue damage. In this article we present the research findings that strongly support a biopsychosocial concept of chronic pain, describe the current best evidence for management strategies and suggest a common general pathway for all types of chronic pain. The principles of management of some of the most important or frequently encountered chronic pain problems in paediatric practice; neuropathic pain, complex regional pain syndrome (CRPS), musculoskeletal pain, abdominal pain and headache are also described.

INTRODUCTION
Chronic pain is generally defined as any continuous or recurrent pain lasting more than 12 weeks, or pain that persists beyond the normal expected time for tissue healing; causes may be postinjury, disease-related or idiopathic. Prevalence rates for idiopathic pain range substantially in community surveys (eg, headache: 8–83%; abdominal pain: 4–53%; back pain: 14–24%; musculoskeletal pain: 4–40%), they are generally higher in girls and increase with age.1 Similar high rates are reported for disease related pain; for example, in children with polyarticular arthritis 76% reported pain on >60% of days despite treatment with methotrexate, tumour necrosis factor-α inhibitors or both.2 Identification and management of chronic pain of any aetiology is important because of its striking association with characteristic behaviours and negative effects on everyday functioning that are not only harmful and distressing in themselves, but may also delay or prevent recovery and contribute to poor long-term prognosis. These behaviours and effects are sometimes described as ‘chronic pain syndrome’ although the term does not clarify diagnosis.

The management of chronic pain in children is frequently challenging, not least because the complex relationships between chronic pain, illness and health are often poorly appreciated and understood by patients and clinicians. Below we describe the pathophysiology, presentation, principles of assessment and management of chronic pain and suggest a general pathway for care. Additional references and recommendations for further reading are provided as online supporting materials.
A number of chronic pain conditions have found significant changes in structure and functional connectivity compared with controls. The role of CNS plasticity in long-term pain, the regulation of pain during development and neuropathic pain in children have all been reviewed recently.

Sleep disturbance, anxiety and mood disorders are common comorbid problems in children with chronic pain. Compared to controls, children and adolescents with pain due to JIA, sickle cell disease, migraine/headache, functional abdominal pain, juvenile fibromyalgia syndrome, chronic musculoskeletal pain and mixed causes, all suffered from clinically damaging sleep impairment. Disordered sleep and pain sensitivity are closely inter-related, and studies show that treatment of sleep problems may improve pain symptoms, analgesic effectiveness, mood and quality of life. Clinically elevated levels of anxiety were reported in children with non-cardiac chest pain (56–81%), juvenile fibromyalgia (58%) and abdominal pain (45–79%). Chronic pain is also a risk factor for suicidal ideation in adolescents. Significant pain-related impairment of daily functioning, particularly school attendance, shows clear relationships with pain intensity, psychological and emotional functioning.

Given the importance of pain as a mechanism for survival, it is perhaps unsurprising that pain perception is clearly influenced by conscious and unconscious memory, cognitive and emotional functioning and contextual factors that are explicitly included in a biopsychosocial formulation of pain. It follows therefore that as chronic pain is the result of a complex interaction of biological, psychological and socially determined mechanisms, it should be assessed and managed within the framework of these three domains. In addition, it is essential to appreciate that suppression or treatment of underlying disease may not lead to resolution of pain and therefore pain should be managed independently and concurrently.

INITIAL PRESENTATION, ASSESSMENT AND MANAGEMENT PATHWAY
The initial approach to assessment and management is shown in figure 1. The aims are to identify and quantify important symptoms, signs and behaviours indicating possible mechanisms of pain, its impact on functioning, and to identify targets for treatment. Important areas of questioning within the three domains are given in table 1.

The use of instruments such as age-appropriate diagnostic or health screening questionnaires and formal assessments of psychological and physical function are potentially helpful but may not be feasible in general clinics. Importantly, pain should be assessed and managed separately, contemporaneously and in conjunction with any investigations or diagnostic clarification.

Assessment and management are bridged by an individualised biopsychosocial formulation (see below) and a treatment plan that includes pain education, therapeutic interventions as indicated, and the setting of functional outcome goals. Figure 2 shows a common pathway for chronic pain management, regardless of aetiology. Outcome goals should be developmentally appropriate, personally meaningful and negotiated with children and their families, for example, a staged improvement in school attendance and resumption of previously enjoyed activities/social interactions. Reviews should be at predetermined intervals. If progress is unsatisfactory, further evaluation and modification of the management plan may be indicated to identify barriers and refocus interventions. Progress depends on many factors including the complexity and chronicity of the pain problem and associated degree of functional impairment, access to specialist input such as physiotherapy and psychology, and patient and family adherence to interventions. Lack of progress and failure of symptom resolution should lead to referral for specialist, multidisciplinary input (figure 2).

PRINCIPLES OF MANAGEMENT AND INTERVENTIONS
Because the many co-contributing mechanisms to chronic pain are relevant across multiple patient diagnostic groups, common management strategies are often applicable such as a trial of simple analgesics, sleep management and interventions to improve pain coping and restore function, although direct evidence for specific treatments is stronger for certain pain conditions.

The first step is to construct an individual biopsychosocial formulation of pain that is shared with patient and family through pain education; figure 3 gives an example for a child with chronic inflammatory pain. The formulation explains contributing causes of pain and the rationale for management using

Figure 1  Clinical management of paediatric chronic pain on presentation.
pharmacological, physical and psychological interventions, it also helps to establish a constructive therapeutic relationship by acknowledgement, validation and explanation.

*Pain education:* The goal of education is to find a common denominator between current scientific knowledge of the (biopsychosocial) nature of chronic pain and the subjective viewpoint of the child and their family, so that they are better able to cope with pain and engage with management strategies. This includes explanation and reassurance about the cause of pain, a brief summary of relevant pain mechanisms and the integral role of psychosocial and physical factors in precipitating and maintaining pain. The use of therapeutic stories, metaphors, leaflets, books, on-line information resources, ‘apps’ and other audiovisual media can be introduced in a supportive function to consolidate verbally transmitted information. A recent systematic review concluded that cognitive reassurance, that is, providing explanations and education, was associated with higher satisfaction, enablement, reduced concerns directly after the consultation, improvement in symptoms at follow-up and reduced pain.21 Studies have concluded that amitriptyline for other pain conditions is controversial although it is used in adults with fibromyalgia, where it is thought to reduce pain due to effects on central sensitisation, although a recent Cochrane review concluded that a positive effect is likely only in a minority of patients.24 Studies have concluded that amitriptyline is either not effective or there is insufficient evidence to support its use in childhood migraine or functional abdominal pain.22 23 Gabapentin and pregabalin are calcium channel-blocking anticonvulsants with activity against neuropathic pain in adults and children.4 19 They have also been shown experimentally to reduce central sensitisation in adults and consequently have been used in fibromyalgia but there is currently no evidence to support such use in children. Gabapentin may be helpful in childhood refractory insomnia.28 Pregabalin has been shown to be effective in postchemotherapy neuropathic pain.25

**Table 1** Domains of clinical evaluation of chronic pain at presentation

<table>
<thead>
<tr>
<th>Biological</th>
<th>Psychological</th>
<th>Social</th>
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<tr>
<td>Pain characteristics</td>
<td></td>
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<tr>
<td>Site</td>
<td>Mood</td>
<td>School attendance</td>
</tr>
<tr>
<td>Temporal features</td>
<td>Anxiety</td>
<td>Social functioning (peer and family relationships)</td>
</tr>
<tr>
<td>Descriptors</td>
<td>Cognitions (eg, beliefs, attitudes)</td>
<td>Parental behaviour (solicitous or protective responses, minimisation)</td>
</tr>
<tr>
<td>Intensity</td>
<td>Sleep</td>
<td>Parent characteristics</td>
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<tr>
<td>Radiation</td>
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<tr>
<td>Precipitants</td>
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<td>Relieving factors</td>
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<td>Physical functioning</td>
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Neuropathic pain may respond to treatment with drugs that act on neurotransmitters and ion channels that are involved in pain transmission in damaged nervous tissue. Amitriptyline, a tricyclic antidepressant, has a fairly well-established place in the treatment of neuropathic pain in adults where it is considered a first-line therapy in non-specialist settings. Low dose amitriptyline (5–10 mg daily) is also used in children with some types of neuropathic pain, where its sedative effect can also be helpful if there is accompanying disordered sleep.4 20 The use of amitriptyline for other pain conditions is controversial although it is used in adults with fibromyalgia, where it is thought to reduce pain due to effects on central sensitisation, although a recent Cochrane review concluded that a positive effect is likely only in a minority of patients.21 Studies have concluded that amitriptyline is either not effective or there is insufficient evidence to support its use in childhood migraine or functional abdominal pain.22 23

Gabapentin and pregabalin are calcium channel-blocking anticonvulsants with activity against neuropathic pain in adults and children.4 19 They have also been shown experimentally to reduce central sensitisation in adults and consequently have been used in fibromyalgia but there is currently no evidence to support such use in children. Gabapentin may be helpful in childhood refractory insomnia.28 Pregabalin has been shown to be effective in postchemotherapy neuropathic pain.25

Overall, the role of pharmacological interventions in children with chronic pain in non-specialist settings is severely limited by lack of research evidence for efficacy and potential side effects. In a number of cases, for example, when opioids administered during a previous acute pain episode have been continued, or in medication-overuse headache, gradual withdrawal (rather than the introduction of new medicines) is indicated as part of the overall treatment strategy.

**Psychological interventions:** A broad number of interventions underpinned by psychological theory and methods, emphasising psychological or social factors rather than biological factors, are included under the umbrella term psychological interventions. Primary interventions that are currently used include multicomponent cognitive behavioural therapy augmented by strategies such as relaxation, hypnosis, biofeedback and operant strategies...
Aimmed at parents. Other self-management interventions commonly delivered within a cognitive behavioural framework include pacing and sleep hygiene.

A recent systematic review found psychological treatments to be effective in reducing pain intensity for headache and also improved pain and disability in non-headache pain (including JIA and sickle cell disease). Evidence is limited to estimate the effects of psychological therapies on mood and also for effects on disability in children with headache. The inclusion of parents, significantly improves child symptoms for painful
conditions immediately post-treatment. Studies directly comparing self-administered versus therapist-administered interventions have found similar effects on pain reduction.

‘Pacing’ is regularly recommended and involves individuals learning to balance time spent on activity and rest in order to achieve increased function/participation in meaningful activities. However, the concept currently lacks consensus definition and demonstrable evidence base as a stand-alone intervention.

Sleep management primarily involves identifying poor sleep hygiene patterns and implementing strategies to improve sleep regulation.

Physical interventions include but are not limited to physiotherapy, massage therapy and desensitisation treatments, transcutaneous electrical nerve stimulation (TENS), local heat and cold (thermal analgesia), acupuncture and mirror box therapy. The rationale for physiotherapy in chronic pain stems from evidence of the beneficial effects of exercise on tissue healing, function and mood coupled with the belief that activity avoidance and resultant deconditioning contribute to ongoing pain by encouraging a negative cycle of decreasing function and increasing pain. Research studies tend to report physical interventions as part of multimodal pain management, including psychological and pharmacological techniques rather than trials of clearly defined physiotherapeutic techniques such as progressive muscle strengthening, graded motor imagery, sensory-motor treatment or in vivo graded exposure alone. Physiotherapy has an established place as a component of multidisciplinary management of childhood chronic pain, especially in the management of musculoskeletal pain and complex regional pain syndrome (CRPS). Acupuncture and other forms of complementary medicine are used in some centres, and even though children and families often report that such treatments are helpful, evidence is otherwise lacking. Mirror box therapy is a relatively novel sensorimotor technique for localised pain in a single limb in which patients perform movements of the unaffected limb while watching its mirror reflection superimposed over the (unseen) affected limb, thus creating a visual illusion of affected limb movement. A number of small studies and case reports have found benefit in adults and adolescents with neuropathic phantom limb pain. However, mirror therapy has been shown to have positive and negative effects on the symptoms of CRPS.

**SPECIFIC CHRONIC PAIN CONDITIONS**

**Neuropathic pain** is defined as pain that is due to a lesion or disease of the somatosensory nervous system, its causes, assessment and management in childhood have been reviewed recently. Neuropathic pain may coexist with nociceptive/inflammatory pain; causes include traumatic injury, cancer, chemotherapy, chronic infection, neurological and metabolic disease, and inherited sensory nerve dysfunction. CRPS II is by definition due to nerve injury, whereas CRPS type I presents a similar clinical picture but without obvious nerve damage. The evidence base for the use of medications and interventions for neuropathic pain in children is weak. Specific pharmacological management potentially includes many systemic and local treatments but as the efficacy and therapeutic index are often relatively low, fairly rapid progression to specialist assistance is recommended if neuropathic pain is suspected or responds poorly to first-line treatment.

**Complex regional pain syndrome** was formerly known as reflex sympathetic dystrophy or causalgia. It is characterised by localised pain with variable swelling, discolouration (vasomotor), abnormal sweating (sudomotor) and dysmorphic changes to hair and nails, usually distally in a single, usually lower, limb. It is rare below the age of 5 years and most frequently seen in girls, peak incidence 14 years. Most commonly there is no obvious precipitating factor. The diagnosis is
often delayed having tried a variety of unhelpful interventions, including immobilisation, consequently children with CRPS can present with significant functional impairment.40 Clinical criteria for diagnosis, validated in adults, may be helpful in reducing diagnostic confusion.41 Severe CRPS can be accompanied by dystonia with strikingly abnormal posture or limb position and sometimes associated movement disorders. The prognosis of childhood CRPS is good, although relapses are common (25–40%); delay in diagnosis and inappropriate treatment may adversely affect prognosis.42

Following assessment, interventions favouring mobilisation or remobilisation of the affected limb are universally held to be important. Early referral to an appropriately experienced physiotherapist and other physical interventions such as desensitisation and TENS are indicated along with pharmacological and psychological interventions such as simple analgesics and distraction to improve the tolerability of painful exercises. Amitriptyline, gabapentin and other agents active in neuropathic pain are sometimes also used empirically for CRPS. Failure to progress or worsening of symptoms and disability are likely to be multifactorial and should trigger specialist referral for multidisciplinary assessment and management.19 Although physiotherapy is often held to be key, there have been few good studies analysing the contribution of different elements of care and most specialist treatment programmes for CRPS offer a package of physical, psychological and pharmacological strategies.31

**Chronic Musculoskeletal Pain** that is either generalised or localised (eg, low back pain or joint pain) can lead to significant functional impairment, it may be disease-related, persisting after treatment of joint inflammation or trauma, or there may be no clear cause.32 41 Adolescents with chronic widespread musculoskeletal pain, sometimes called juvenile fibromyalgia or diffuse idiopathic pain are increasingly presenting for treatment, characteristically, they have pain at multiple sites, poor physical functioning, disturbed sleep, fatigue and low mood. Again, initial assessment (figure 1) should focus on clarification of the diagnosis and confirmation that any underlying treatable inflammatory or other cause of pain is optimally managed. Partly correctable biomechanical factors may contribute such as poor posture, flat feet, leg length discrepancy, deconditioning (reduced muscle strength and endurance) and obesity, in addition joint hypermobility (the presence of increased mobility in 6 or more joints) has been associated with musculoskeletal pain in some populations.44–46 Recent reviews have emphasised biospsychosocial formulations of pain and the importance of pain education for children and their families as a part of management.42 43

Simple analgesics (paracetamol and NSAIDs) have usually been tried by families and found to be ineffective. Opioids can contribute to lethargy and fatigue and are not indicated. A trial of amitriptyline or gabapentin may be logical if central sensitisation is thought to be playing a role, although there are no studies to support this strategy. A rehabilitative approach using sleep management, functional targets, graded or paced aerobic exercise therapy with targeted muscle strengthening are most often used together with psychological strategies for the management of pain, anxiety or low mood (figure 2).

**Headaches** are common during childhood, population prevalence estimates range from 8–83%.1 Primary headache disorders are predominantly migraine and tension-type headache. Secondary headache due to central nervous system lesions, infection or other pathology should be excluded (figure 1). A minority of children with primary headache report daily headaches and significant disability. Migraine headaches differ from those in adults (no aura) and migraine variants are more common, for example, ophthalmoplegic or complex migraine with transient neurological abnormalities.

Primary headache is usually amenable to patient and family education, removal of possible triggers and judicious use of simple analgesics. Specific therapies and prophylaxis for migraine such as triptans and β-blockers are also used but have not been subjected to rigorous evaluation in children.44 Further interventions such as sleep management, increased physical activity, school attendance and changed dietary habits, including adequate hydration, are often recommended.47 48 Psychological therapies are effective for primary headache. Recent meta-analyses support relaxation training for recurrent headache; a large positive effect on pain reduction at immediate post-treatment and follow-up was found, whereas there were small and non-significant effects on disability and emotional functioning.26 49 Long-term improvements over more than 3 years after treatment with relaxation, for tension-type as well as migraine headaches, have also been shown. Recently, applied relaxation has been presented via the Internet to children and adolescents with recurrent headache with positive effects.50

**Chronic or recurrent abdominal pain (CAP)** is defined as at least 3 pain episodes over at least 3 months interfering with function. The incidence of CAP peaks between ages 4 to 6 years and again in early adolescence (particularly girls >12 years). Significant ongoing pain is usually medically investigated in order to identify directly treatable causes such as inflammatory bowel disease, but the cause often remains obscure (figure 1). Clinical guidelines on the investigation and management of CAP including ‘red flag’ symptoms of organic disease and ongoing management are available.51 Functional gastrointestinal disease (FGID) is classified according to Rome III criteria. A recent study identified prognostic subgroups of FGID associated with CAP based on pain severity and psychosocial variables at first assessment: children with high levels of pain, poor pain coping, negative affect, pain catastrophising and higher levels of functional disability with evidence of central sensitisation had the worst long-term prognosis.52

As before, the principles underpinning the treatment of CAP emphasise a biospsychosocial formulation of pain together with pain education and targeted interventions. Symptoms are sometimes associated with specific foods, and eating is frequently cited as a pain trigger in FGID. Peppermint oil supplements for 2 weeks reduced symptoms in children with irritable bowel syndrome in one RCT.53 Amitriptyline was equivalent to placebo in one study, and a systematic review has concluded that there is little evidence to support the use of analgesics or other drug treatments.54 55 There is inconclusive evidence that a lactose-free diet decreases symptoms or that a fibre supplement decreases the frequency of pain attacks.56 Well-designed clinical trials and accumulated clinical experience support the view that hypnosis, as an integral part of biospsychosocial management, is the most efficacious treatment for CAP improving pain and disability outcomes.57 Long-term follow-up has shown that the beneficial effects remain even up to 5 years after the intervention in the majority of patients.58

**CONCLUSION**

Chronic pain in children and young people remains an entity which is often poorly recognised, evaluated and managed leading to unnecessary distress and poor health outcomes. In addition to the significant cost to a child’s quality of life, the economic burden of chronic pain in young people in the UK was estimated in 2005 to be approximately £8000 per child per year.59 Progress in the development and investigation of novel treatments for childhood chronic pain remains slow in comparison with other chronic health problems.
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Presentation and management of chronic pain

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