



Relieving Persistent Pain, Improving Health Outcomes

Summary

- Experiencing 'normal' pain is protective. It helps people avoid harm and aids recovery from injury. But maladaptive persistent pain stems from causes such as nervous system injury and abnormal sensitivity, and is not protective.
- Psychological factors play a demonstrable role in determining physical pain thresholds. Social deprivation and variables such as income inequalities may also influence individuals' vulnerability to chronic pain through psychological mechanisms and stress related biological reactions.
- Experiencing pain is central to the harm caused by many forms of ill health, including arthritis, diabetes, depression and cancer. Alleviating pain as a symptom is a vital medical and pharmaceutical care responsibility. However, persistent or chronic pain can also be seen as a condition in its own right. It demands specific bio-medical, psychological and social treatment and care.
- Pain is very prevalent and costly to individuals, communities and society as a whole. About twenty per cent of the UK population is living with significant pain. At any one time a million people in this country have persistent pain which could have been prevented or better treated.
- The cost of pain to British society can be realistically estimated at over £10 billion per annum. The data available suggests that the NHS could cost effectively allocate an additional £1 billion a year to better pain management services in specialist and other settings, such as community pharmacy.
- Specialist pain services bring together multidisciplinary teams containing especially skilled doctors, nurses, physiotherapists, psychologists, pharmacists and other professionals to help people with severe and intractable pain obtain better relief. There are about 200 such services in England at present. But access times and standards of care are variable – some patients in need may have to wait for a year or more. Even with extra investment, specialist services cannot serve the majority of people in need of better pain treatment and care.
- Public health programmes can contribute to prevention and facilitate improved self care through enhancing public and professional understanding of persistent pain as a medical and psycho-social problem. In Australia a television campaign encouraged people to stay active in spite of experiencing pain. This reduced national sickness absence rates. Public health expertise might also contribute to an improved understanding of the prevalence of pain and service development issues.
- Pain relief performance measures could be incorporated into the NICE managed Quality and Outcomes Framework for GPs and other NHS contractual agreements, to incentivise the pursuit of better pain related health outcomes.
- There is evidence that the education of health professionals such as doctors and pharmacists needs to be improved in ways that will permit a better 'whole system' understanding of persistent pain and associated risk factors. An increased use of pain assessment instruments in primary care is an example of good practice that could assist in identifying individuals who are 'at risk', and in finding early stage persistent pain cases.
- Community pharmacy based services could play a key role in extending access to effective pain relief via supporting the appropriate use of all types of medicines and facilitating access to other proven therapies, including physiotherapy and cognitive behavioural therapy designed for pain management.
- Continuing pharmaceutical innovation has a vital role to play in further improving pain related health outcomes, and preventing or modifying the course of diseases that cause pain. Failures to use new and existing medicines as effectively as possible to control pain undermine patient interests. They also risk impairing the future funding of pharmaceutical research. This would in the longer term increase rather than reduce care costs, and/or damage the capacity of societies such as that of the UK to fund welfare services.

Introduction

Relieving pain has been a central goal of medicine, and for humanity as a whole, throughout history.¹ There is evidence, for example, that opium was used to alleviate suffering some 5,000 years ago in and around what is today Iraq, while the ancient Egyptians and Chinese (and subsequently Hippocrates, who was born on the Greek island of Kos over 400 years before Christ) knew of the analgesic properties of White Willow bark. The active ingredient of the latter is today termed salicin. It is closely related to aspirin.

Yet despite the long history of analgesia in medical and pharmaceutical care, specialised pain management for both adults and children is a relatively new discipline. The appreciation of pain as a public health issue is even more recent. There remain many unresolved problems relating to its prevention and treatment. As a result, many people are still living and dying in avoidable distress. However, in recent years patients and their representatives, health professionals and Governments have become more aware of the scale of the impacts of pain on individuals and communities. Improving understanding and alleviation of both acute and chronic pain (which may be seen as a discrete form of disease in its own right) has become a priority for health policy makers and health professionals alike.

Prevalence estimates vary, and it is arguably unhelpful to quote what may on occasions seem to be exaggerated statistics. Nevertheless, the available research indicates that around one in five adults is at any one time suffering from an appreciable level of pain, while every year approaching one person in every ten develops a form of chronic pain (International Association for the Study of Pain, 2004). Furthermore, persistent pain threatens to impose an increased burden in ageing populations across the world. This is because of the rising prevalence of not only conditions such as osteoarthritis and cancer, but also because of rises in the numbers of individuals with disorders such as diabetes (which can damage nerve pathways) and depression, which may lower experienced pain thresholds. Increasing rates of survival following major surgical interventions are also adding to the numbers of people developing long term pain.

A seminal initiative to establish a comprehensive national pain strategy took place in Australia in 2010. This involved holding a 'Summit', and led on there to the establishment of a multidisciplinary Faculty of Pain Medicine, a Chapter of Palliative Medicine and the formation of a standing 'lobbying' organisation – Pain Australia. Subsequent steps forward in other settings have included the publication of a Canadian Pain Strategy and the holding of an inaugural International Pain Summit, led by the International Association for the Study of Pain (IASP). The resulting *Declaration*

of Montreal described access to effective pain management as a fundamental human right, and argued that all governments and health care institutions have an obligation to establish laws, policies, and systems that will help promote the universal availability of good pain management services (International Association for the Study of Pain, 2010). Another landmark document was produced in 2011 by the US Institute of Medicine (IoM). Entitled *Relieving Pain in America*, this work is intended to have a transformation impact on pain care for all groups in US society (Institute of Medicine, 2011).

In the UK, the Royal College of Anaesthetists established a Faculty of Pain Medicine in 2007, and the 2008 Chief Medical Officer for England's report (Chief Medical Officer, 2008) highlighted the extent of chronic pain and its impact on individuals, families and the overall economy (Box 1).

Box 1: The economics of pain

Quantifying the economic burdens imposed by all forms of disease is important, because it can inform policy makers about scale of the investments it is appropriate to make in their alleviation (Phillips, et al., 2008). However, the methods available for undertaking such calculations are often relatively crude. In the case of persistent pain the situation is complicated by the fact that although in some instances of neurological damage and/or abnormal functional sensitivity pain is the only defining characteristic of the condition being considered, in many other contexts it is just one aspect of a wider set of impairments and disabilities. Attributing a specific cost to pain *per se* in such circumstances is inherently problematic.

Other similar challenges range from the limitations of using days of recorded sickness absence as a measure of lost productivity through to the difficulty of measuring the economic impact of disabling complaints in population groups that do not have formal employment. In the former case, for example, it is on the one hand uncertain in societies with significant numbers of unemployed people and high levels of publicly funded unemployment and disability benefit how much any given period away from work on average costs the overall community. It may be less than is typically assumed. On the other, it is important not to neglect the hidden costs of 'morbid presenteeism'. Pain experienced at work can reduce performance and impose real costs without resulting in absence.

To the extent that pain decreases the benefits of leisure and may impair self care, the burdens it imposes on groups such as retired people and those around them are also likely to be large but unrecorded. However, having acknowledged such issues the available data indicates that the overall cost of long term conditions like back pain, together with painful disorders such as migraine and post surgical chronic pain, is likely to be in excess of £10 billion per annum (Phillips 2001). That is, it is approaching one per cent of GDP, even excluding factors such as directly incurred health care costs. Such figures underline the potential rewards to be gained from providing more effective chronic pain prevention and treatment services.

1 The English term 'pain' is derived from the name of the Greek spirit (or 'Goddess') of revenge and retribution, Poine. The idea that humanity suffers because of sins and crimes, and escapes pain through acts of virtue and compensation, is deeply rooted in ancient history. It may even today sometimes underlie the stigmatisation of people suffering pain – see main text.

Important progress has already been achieved in Scotland, while in November 2011 the UK Chronic Pain Coalition (CPC) organised a Summit meeting similar to the original Australian initiative in London for policymakers, health care commissioners, health care providers and patient representatives. Its objectives were to raise awareness of the extent of the problem of chronic pain, highlight opportunities and challenges for service development, and to where possible build consensus around the interventions and service models needed to improve pain related health outcomes.

Against this background the goals of this UCL School of Pharmacy report include assessing the case for investing further resources in improving the management of acute and chronic pain, and analysing the ways in which community and other pharmacists could in future contribute to further outcome improvements in this field. (There is evidence that pain is an area in which a majority of people already seek help from pharmacists, and expect them to have a special expertise – Woolf et al 2008, Carr 2011, Hamell Communications 2011.) It also aims to contribute to public and professional understanding of different types of pain and its treatment, from both a clinically oriented and a public health – population level – perspective, and discusses issues such as the costs and benefits of using opioid (morphine like) and other medicines to help manage what is frequently a social and psychological, rather than just a conventionally biomedical, set of personal and community challenges.

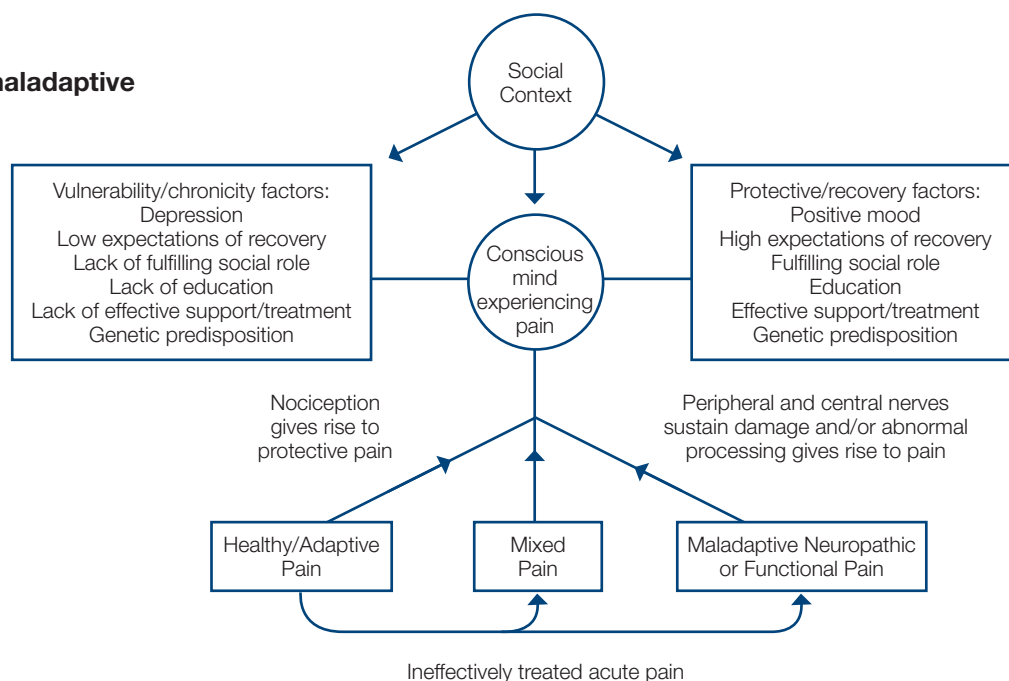
At present, there are a number of areas where further research is needed on the extent of the problems that pain causes for people in countries such as the UK and the potential for different types of intervention cost effectively to relieve them. But the analysis offered below indicates that at any one time it can be conservatively estimated that there are a million people in this country who are living in significant pain, yet whose condition could have either been prevented or be being better treated.

There is a powerful case for increasing the proportion of NHS and other social resources devoted to these ends, albeit that in a period of austerity increased financial investment in any public service area will have to be balanced by reductions in spending elsewhere. However, to the extent that better public and professional understanding and commitment to effective pain prevention and relief can be achieved through better practices and improved use of existing public and private resources, this will deliver increased welfare in ways which will not impose further costs and could in some circumstances permit the release of funding and/or help foster economic growth. Developing the capacity of community pharmacy within primary care to further control pain as both an individual level and a public health problem could in future provide an important example of this type of progress.

The causes and occurrence of pain

The International Association for the Study of Pain (IASP) defines pain as *'an unpleasant sensory and emotional experience associated with actual or potential tissue damage'* (International Association for the Study of Pain, 2004). It is a multi-dimensional sensory experience which may vary in intensity, quality, duration and referral. Adaptive (acute) pain contributes to the survival of the species by protecting from injury and promoting healing. Consciously experiencing it teaches animals of all types to avoid potential harm, and to avoid further damage to recovering tissue. By contrast, maladaptive pain (which is termed persistent or chronic in this UCL School of Pharmacy report) may be defined as having lost its connection with its original cause and is the result of abnormal sensory processing. Figure 1 provides an overview of this basic distinction between 'healthy' (adaptive) and pathological (maladaptive) forms of pain. It also outlines the possible linkages between mental and physical suffering, and how initially adaptive responses may over time become counter-productive.

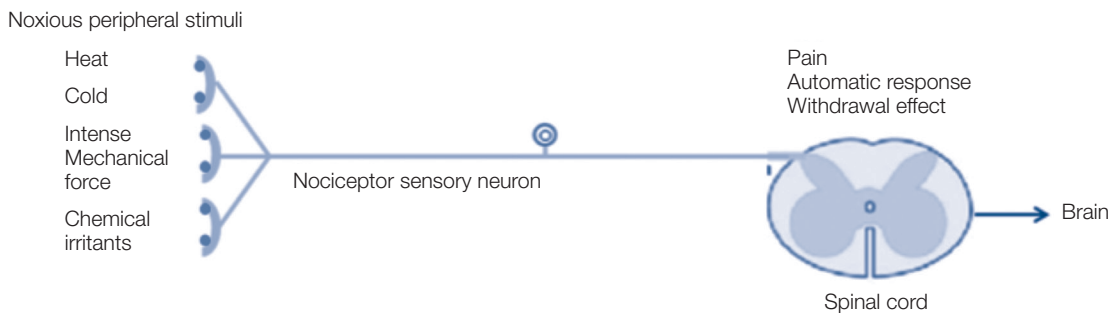
Figure 1: Adaptive and maladaptive pain – an overview.



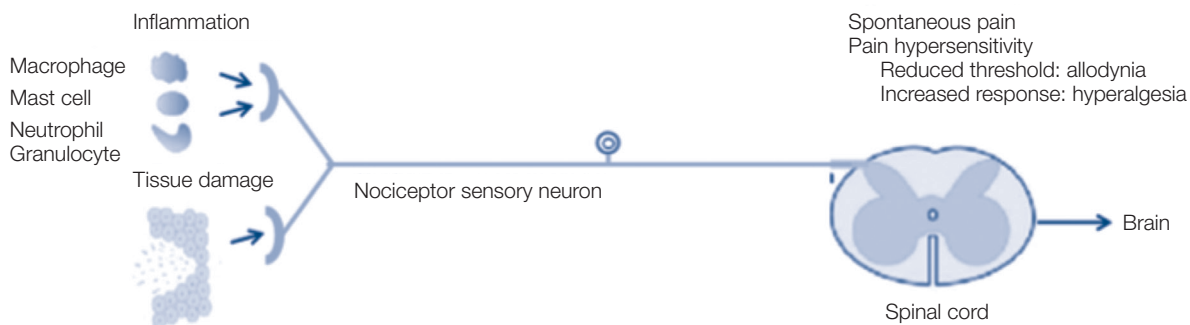
Source: The authors

Figure 2. The four primary types of pain.

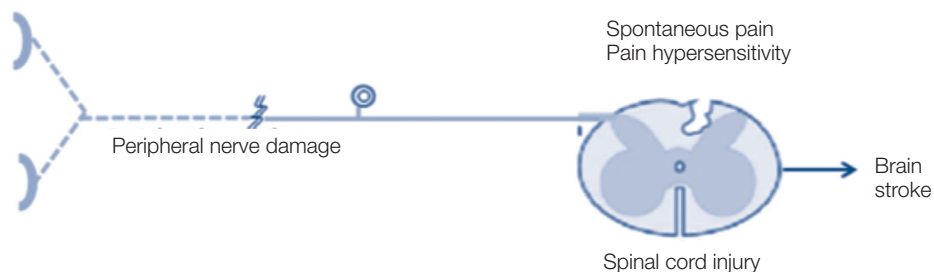
A. Nociceptive pain



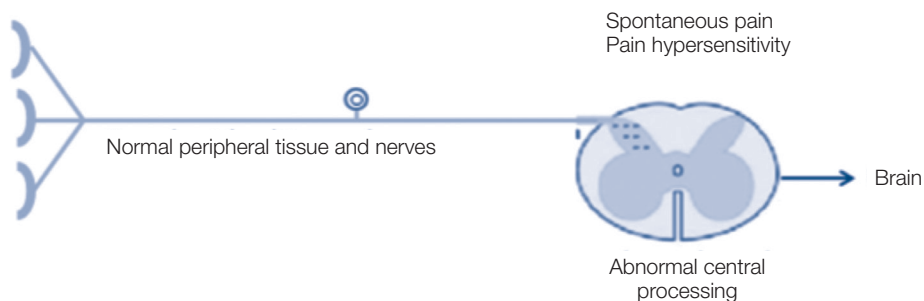
B. Inflammatory pain



C. Neuropathic pain



D. Functional pain



Source: Woolf (2004).

Note: Nociceptive pain is initiated by noxious thermal, mechanical or chemical stimuli. Inflammatory pain is initiated by inflammatory cytokines acting on nociceptors to produce spontaneous pain and 'normal hypersensitivity'. Neuropathic pain is caused by nerve damage either in the peripheral or central nervous systems. Functional pain is caused purely by abnormal central processing in the brain and spinal cord.

As Figure 2 shows, pain can be further divided into four categories: nociceptive, inflammatory, neuropathic and functional pain (Woolf, 2004). The feeling of acute pain caused by a noxious (harmful) mechanical, thermal or chemical stimulus is controlled by the nociceptive² system. This extends from receptors located in the skin via nerves running into the spinal cord and up the brain stem, and from there via the thalamus to the cerebral cortex. It is probably in the thalamus and the 'thinking'/cortical area of the brain that the sensation of pain is experienced and analysed. Nociceptive pain system failures are rare but when they occur they can result in non-volitional self-induced tissue damage and a reduced life expectancy, as can be seen in patients with congenital – genetically caused – insensitivity to pain (Nagasakoa et al., 2003).

Tissue damage occurring through, for example, accidents, surgery or inflammatory diseases, causes responses that involve a shift in emphasis from protecting against noxious stimuli while living normally to promoting the healing of the injured tissue. Inflammatory pain is associated with an increase in sensitivity in the affected area, so that stimuli that do not cause pain in an every-day setting can become intolerable. The functional effect of this is that injured areas are less likely to be exposed to further damage until healing is complete. In the care of people with long term conditions such as, say, rheumatoid or osteoarthritis a key aim of therapy is to reduce inflammatory pain to tolerable levels without

removing or depressing the nociceptive warning system, or impairing useful healing processes (Woolf, 2004).

Neuropathic and functional pain are both types of maladaptive pain which have become uncoupled from a noxious stimulus or tissue healing process. Neuropathic pain is the result of damage to either the peripheral or central nervous systems (that is, the PNS and the CNS respectively). Peripheral neuropathy is due to nerve lesions and may occur in patients with diabetes or HIV/AIDS, or in individuals suffering from post-herpetic neuralgia caused by shingles (Table 1). Damage to the CNS in patients with spinal cord injuries and conditions such as multiple sclerosis or stroke can cause central neuropathic pain.

Functional pain is not caused by a neurological deficit or peripheral abnormality but an abnormal responsiveness or function of the nervous system where heightened sensitivity amplifies the sensation of pain in circumstances where it would not normally be experienced as problematic. There are several common conditions that have functional pain features, including fibromyalgia (see Box 2) and irritable bowel syndrome. This form of pain can be thought of as resulting from either the chronic activation of pain receptor sensitivity in circumstances where it is not protective, or other changes in the spinal column or brain which allow pain signals to be experienced as significantly more hurtful than would normally be the case.

2 Noci is the Latin word for causing harm, injury or pain

Table 1. Types of persistent pain, their symptoms and their pharmaceutical treatment options

Condition	Type of Pain	Pain Symptoms	Physiology	Pharmacological Treatment
Fibromyalgia	Functional	Deep muscular aching, throbbing, shooting, stabbing or intense burning	Abnormal central processing	Antidepressants (Amitryptaline/Duloxetine) or anticonvulsants (Pregabalin/Gabapentin)
Diabetic Neuropathy	Neuropathic	Tingling, numbness, burning	Peripheral nerve damage	Antidepressants or anticonvulsants
Osteoarthritis	Inflammatory	Joint pain	Inflammatory tissue damage causes increased pain sensitivity	Paracetamol, topical and oral NSAIDS, coxibs or opioids if other treatments unsuccessful
Rheumatoid arthritis	Inflammatory	Aching, throbbing pain. Hot, swollen joints	Inflammatory tissue damage causes increased pain sensitivity	Disease modifying agents plus Paracetamol. NSAID or Coxibs at lowest effective dose for shortest possible time.
Post-herpetic neuralgia	Neuropathic	Burning, throbbing, tingling, stabbing, piercing, shooting, sharp or aching. May include allodynia	Nerve damage and sensitisation	Topical lidocaine, topical capsaicin, Anticonvulsants (Gabapentin/Pregabalin)
Cancer-related	Mixed nociceptive, inflammatory and neuropathic	Could involve any of the symptoms of nociceptive, inflammatory or neuropathic pain	Nerve damage, inflammation caused by treatment or tumour growth	Dependent on cause of pain, may involve opioids and/or other drugs

Box 2: Fibromyalgia

Fibromyalgia, which reportedly affects about 2 per cent of the adult population, involves widespread pain and tenderness. The main symptoms include multifocal pain, fatigue, insomnia, problems with thinking and memory and other psychological distress. Patients may also experience stiffness, poor balance, headaches and impaired physical function (Smith et al., 2011). The precise aetiology is unknown. But it in part involves altered functioning in central ascending and descending pain processing pathways. Genetic and peripheral nervous system linked factors are also implicated.

People with fibromyalgia have been shown to have increased levels of pain associated neurotransmitters such as substance P, and a reduction in reward-linked substances like dopamine. This may be due to their prolonged exposure to stress. No single treatment therapy has been found to be universally effective, which may indicate that this diagnosis embodies numerous sub-conditions. Licensed pharmaceutical care options include antidepressants such as duloxetine (a serotonin and nor-adrenaline reuptake inhibitor) and pregabalin, a voltage gated calcium channel blocker. Other non-licensed alternatives exist. Non-pharmacological approaches such as exercise, education and cognitive-behavioural therapy (CBT) have been shown to have a positive impact on fibromyalgia. The available data suggests that these options are relatively under-used.

There are in addition other types of pain that do not fit neatly into the four categories outlined above, but may be thought of as involving atypically complex forms of pain causation. For example, migraine is an episodic neurological condition related to abnormal cortical activity which alters sensory activity levels and processing patterns in the brain stem. It involves aspects of functional and inflammatory pain, as well as neurological dysfunction. Cancer related pain can also be due to multiple sources. Its occurrence depends on the tumour involved, its location and its proximity to other tissues. It may also be linked to the surgical and pharmaceutical treatments given, such as the potentially neurotoxic side effects of chemotherapy. Aspects of the control of cancer pain are discussed further in Box 3.

Pain mechanisms

It would be beyond the scope of this brief report to explore in detail the specific mechanisms underlying the various types of pain outlined above. However, the following observations are of particular importance in relation to understanding effective pain management:

- Nociceptive pain involves the opening of ion channels, which cause action potentials to be initiated in the relevant nerves (transduction). These are conducted along the nerve axons to synapses (nerve junctions) located at the dorsal root of the spinal cord. The key excitatory neurotransmitter at these synapses is glutamate. Its release causes action potential transmission to the nociceptive projection neurones which ascend to the brain in the

Box 3: Controlling pain in cancer and improving end of life care

Cancer is often associated with severe pain that can if inadequately treated make a patient's life unbearable (Ddungu, 2011). Yet modern pain management techniques provide relief in virtually every case, when applied with sufficient expertise. A key target of the 2008 World Cancer Declaration was to make effective pain control more accessible on a global basis (Cavalli, 2008). Relieving end of life distress and facilitating 'good deaths' is arguably one of the most important outcomes that high quality health can achieve, even though conventional health economic assessment methods may not always reflect this judgement.

Despite recent service improvements in England and elsewhere there is strong evidence that cancer pain is often undertreated (Pain Australia, 2010). The prevalence of reported pain ranges from 30-50 per cent in people undergoing long term oncological treatment, and may increase to more than 70 per cent in those with advanced cancer (Ddungu, 2011).

The mainstay of cancer pain treatment has for many years been the WHO analgesic ladder and the use of opioids. However, there are now calls for more innovative approaches in this and other end of life and severe pain care contexts – see main text. New NICE clinical guidelines for use in palliative care are currently under consultation (NICE, 2011). The British Pain Society has called for the holistic treatment of cancer patients who are in pain, combining as and when needed psychological support, social support, rehabilitative care and pain management in order to provide the best achievable quality of life (The British Pain Society, 2010).

There is evidence from North America and European countries alike that the prevalence of cancer treatment survivors has tripled over the last three to four decades. This positive trend has been linked to a rise in the number of people suffering from post-treatment pain syndromes. The latter can be caused by chemotherapy, radiation and/or surgery, and are often more complex than other persistent pain syndromes. They can occur up to 20 years post-treatment, and may be under-reported because patients fear that pain is a negative prognostic indicator (Burton et al., 2007). It is also possible that a proportion of people living in pain who do not have a neoplastic disorder may not report their condition because of fears that it may be cancer.

Preventing post-cancer persistent pain should begin with the efficient control of acute pain at the time of diagnosis, and throughout all subsequent treatment processes. The treatment of post-cancer persistent pain remains an evolving competency. It should apply current best practices from the treatment of other persistent pain conditions with cancer specific therapeutic skills (Burton et al., 2007).

spinothalamic tract. Pain signals are subsequently transmitted via the brain stem and the thalamus to other areas of the brain, including not only the cerebral cortex but also the limbic system. This last is the emotional centre of the brain. This helps to explain how the emotions that can accompany

pain, such as fear, anxiety and frustration, are produced (Woolf, 2004), and may be relevant to links observable between chronic physical pain and forms of mental illness.

- If despite nociceptive 'early warnings' body tissues are damaged, factors such as cytokines are produced by inflammatory cells at the sites concerned. Some of these act directly on nociceptors to produce immediate pain, whilst others (like prostaglandin E₂ and nerve growth factor or NGF) serve to promote hypersensitivity to future stimuli. This process is termed peripheral sensitisation. It plays a key role in pain felt in contexts such as the early stages of post-herpetic neuralgia, and in some cases of maladaptive persistent pain.
- In addition to peripheral sensitisation, central sensitisation can also occur. This involves the facilitation and amplification of pain signal transmission in the spine. The phosphorylation (the chemical addition of a phosphate group, which may activate or deactivate a protein) of ion channels and receptors and the induction of various genes changes nerve cell functioning. One of the key receptors to be phosphorylated during central sensitisation is the glutamate-activated NMDA receptor. As a result nerve cells may either be activated by inputs that are normally too weak to induce a response (allodynia), or in their excited state respond in an exaggerated way to stronger signals (hyperalgesia). Central sensitisation is typically involved in chronic and persistent pain, and conditions such as postoperative pain, migraine, neuropathic pain, fibromyalgia and painful gastrointestinal tract disorders.
- Alongside excitatory mechanisms, there are also inhibitory ones which serve to limit sensory inputs to appropriate levels. In the spinal cord the neurotransmitters glycine and GABA³ play an important role in facilitating such effects. It also contains descending (efferent) pathways that transmit inhibitory signals down from the brain stem. In this context noradrenalin (norepinephrine) and serotonin are the key neurotransmitters. This explains why anti-depressant medicines which serve to boost levels of the latter can be effective treatments for some forms of pain. In patients with peripheral nerve injuries, as in neuropathic pain, there is typically a substantial loss of inhibitory mechanisms, particularly those mediated by GABA.

As discussed earlier, there are multiple physiological changes that occur when pain moves from its acute/adaptive form to a persistent/maladaptive type. But modern understandings of pain and its effective management also stress the importance of social and psychological variables, and their impacts on the conscious experience of pain. The interpretation of pain signals can be influenced by factors ranging from past experiences and beliefs to an individual's current

mental state and learned coping strategies. Hence as pain progresses away from being an acute, essentially protective, phenomenon towards being a chronic disease, psychosocial factors become increasingly relevant. Some psychologists may even argue that chronic pain is purely psychogenic in nature, and that it serves as a protective distraction that keeps dangerous emotions at bay. Yet although this might well be so in a proportion of cases it appears probable that in others persistent pain is of primarily bio-mechanical origin, and that associated psychological and social problems result from it rather than cause it.

Chronic pain can result in severe impairments in an individuals' sense of wellbeing, level of function, ability to sleep and general quality of life. Feelings such as depression, anger, hopelessness and despair are reportedly common, and people with persistent pain can become inactive and socially isolated and/or withdrawn. This may on occasions be because of fears that they will do themselves harm through attempting to live normally, although the available evidence is that in contexts such as back pain individuals who are able to 'keep going' often enjoy better long term outcomes than others. Notwithstanding the possibility that people with more severe conditions are more likely to fall into the latter group, supporting the efforts of people with persistent pain to live as fully as possible appears to be an inherently desirable approach.

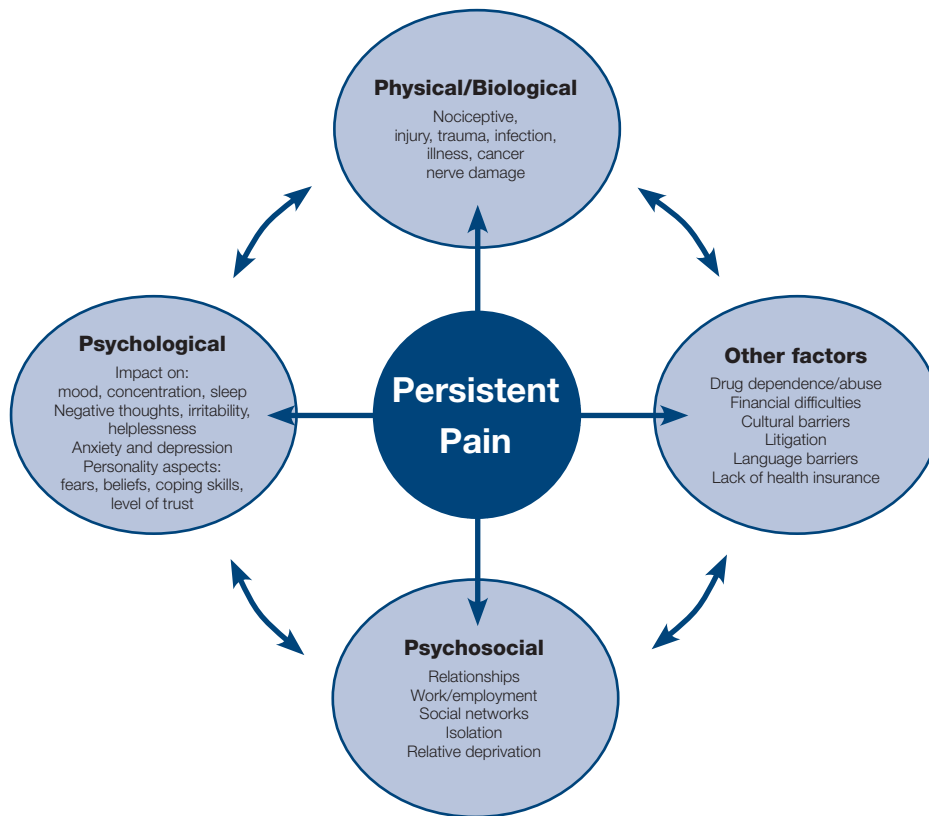
The biopsychosocial model of pain (Figure 3) indicates that the effective prevention and treatment of persistent pain conditions demands that all relevant forms of intervention are employed. In fact, the available evidence suggests that in the back pain context most important factors for determining whether or not acute problems progress towards persistent pain lie in the psychological and environmental domains, although this does not mean that physical pain relief should ever be neglected (Pain Australia, 2010).

At a population level, patterns of non-communicable (non-infectious) diseases seem closely linked to the occurrence of persistent pain, and are in large part determined by the conditions in which people and communities live and work. There are clear links between the observed occurrence of persistent pain, socioeconomic status (Davies et al., 2009) and in communities such as that of the US ethnicity. They arguably mirror the links between socioeconomic status, income disparities and life expectancy found by observers such as Professor Sir Michael Marmot (Marmot et al., 2010).

The allostatic load hypothesis suggests that persistent exposure to adverse social and economic conditions leads to a deleterious accumulation of stress hormones such as cortisol. It is possible that allostatic load could play a part in promoting susceptibility to persistent pain (Goldberg & McGee, 2011). If this proves to be the case it may in future justify further investments in social and psychological, as well as biomedical, approaches to reducing the incidence and prevalence of chronic pain in countries such as Britain.

3 Gamma-aminobutyric acid, the main inhibitory neurotransmitter in all vertebrates. Medicines such as benzodiazepines augment the effects of GABA at many sites in the nervous system.

Figure 3. The Biopsychosocial model of pain.



Source: PainXchange (<http://www.painxchange.com.au/> accessed 10/11/2011).

The epidemiology of pain

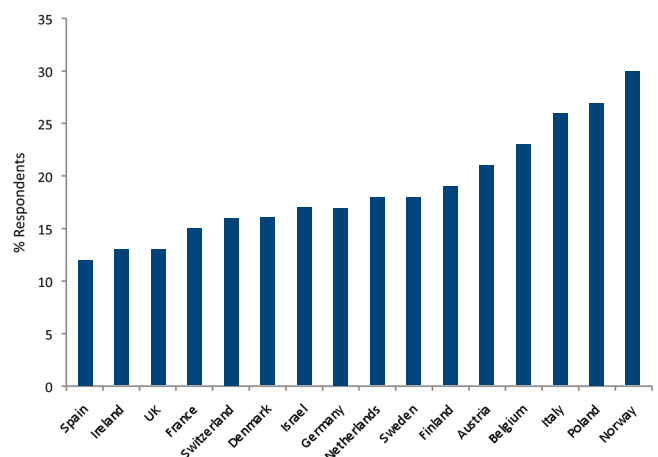
Although further research is in progress, the availability of robust studies of the incidence and prevalence of chronic and other forms of pain in England and elsewhere is limited. Additionally, the studies that have been undertaken may seem to give conflicting results. This is in large part because of the difficulties inherent in finding consistently reproducible ways to measure pain levels within (and across different) communities, in addition to challenges such as that of achieving adequate response rates to telephone and postal surveys. The prevalence rates for persistent pain in the UK quoted in *‘Improving the Current and Future Management of Chronic Pain’* Pain Proposal Committee (2011) range between 13 and 48 per cent. Other sources quote 8 to 60 per cent.

However, analyses such as the Grampian region survey undertaken in the late 1990s (Elliott et al., 1999) and the more recent European survey of persistent pain in Europe (Breivik et al., 2006) provide firm evidence that chronic pain is a widespread problem, which is on many occasions not as well treated as those affected by it would like it to be. In the case of the Scottish research, for instance, the data gathered indicate that a little over 45 per cent of the general population experience some form of chronic pain. Of these the proportion of people suffering the most severe intensity was about 15 per cent (that is, 7 per cent of the general population), compared to almost half reporting

the least severe intensity. At the time this work was undertaken one person in seven said that they had high levels of unmet care need associated with chronic pain.

In the case of the Europe wide investigation by Breivik et al, 46,394 adults from 15 European countries plus Israel were interviewed by telephone. Of the 3800 respondents from the UK, some 13 per cent were found to be suffering from persistent pain, which was well below the overall average observed (Figure 4).

Figure 4. The reported prevalence of persistent pain among adults (>18 years) in 15 European countries and Israel.

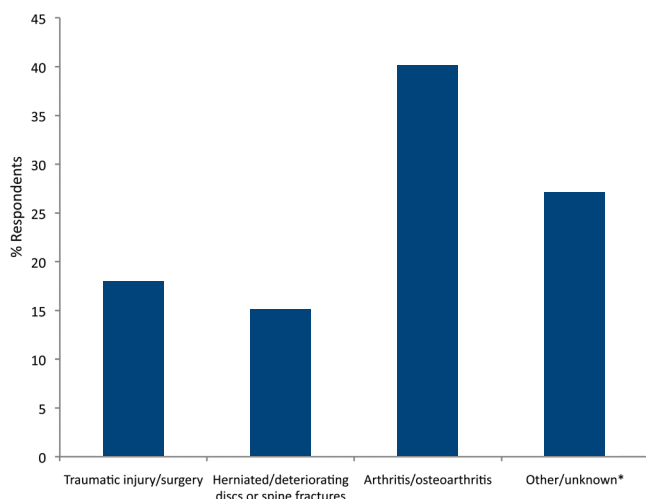


Source: Breivik et al (2006).

That is, 494 of the British survey participants reported suffering from pain for at least six months, and regularly felt pain at least twice a week at a level of five or more on a ten-point numerical rating scale. Of this total, 300 individuals were interviewed in further depth.

The most commonly reported cause of long term pain was broadly defined arthritis, which was responsible for pain in 40 per cent of those who responded (Figure 5). Of those interviewed in depth, just over 30 per cent reported severe pain (that is pain scoring eight, nine or ten on the NRS pain scale) while another third of respondents said they were able to manage their pain on their own. The remainder had not pursued treatment because their pain was intermittent, had reduced naturally, or because they were able to live with it.

Figure 5. Categories of most common types of persistent pain in the UK amongst 272 respondents who answered the question ‘Please tell me the illness or medical condition that is the cause of your pain’ in a telephone interview of persistent pain sufferers.

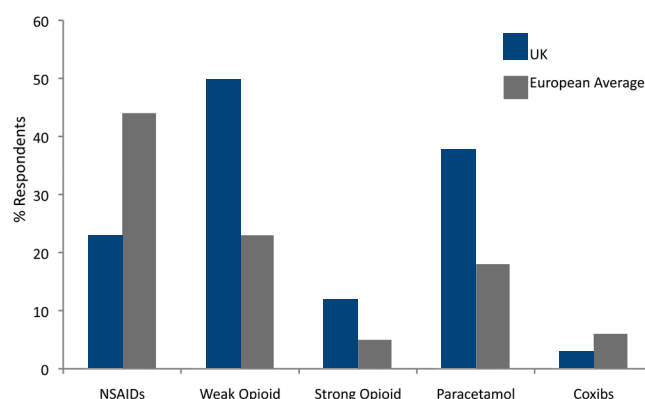


Source: Breivik et al (2006).

* Unlisted causes of pain include multiple sclerosis, Fibromyalgia, migraine, cancer and functional pain of no known origin.

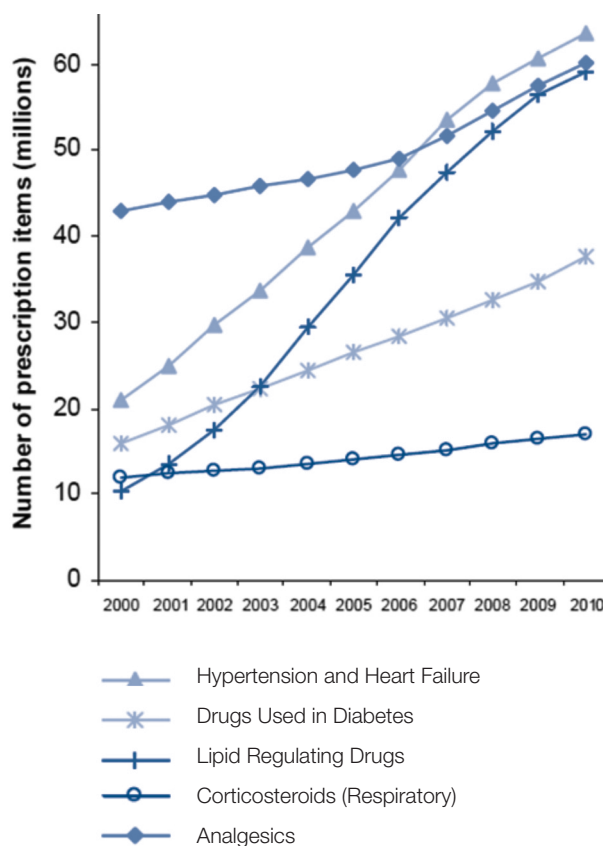
Of those answering the relevant question two thirds said their pain was adequately controlled, albeit that a similar proportion also replied that there were times when the treatment they had been given did not adequately relieve their pain. Figure 6, which is also based on data produced by Breivick et al., suggests that UK patients are twice as likely as average members of the European population to be supplied with drugs classified as weak opioids, and half as likely to be taking non-steroidal anti-inflammatory (NSAID) drugs. One possible implication of such observations is that there is a need for more consistent drug and non-drug treatment guidelines across Europe. Figure 7, which is based on recent prescribing data, describes the increasing volume of analgesic medicine dispensing in the community, which in total now accounts for NHS outlays of over £500 million a year in England alone.

Figure 6. Current (2003) use of prescription medicines in the UK compared with the European average. Answers to the structured interview question ‘which prescription pain medicines are you currently taking for the specific pain we have been discussing?’



Source: Breivik et al (2006).

Figure 7. Ten-year trends in number of prescription items dispensed for the five main medicines groupings with the greatest net ingredient cost in 2010.



Source: The NHS Information Centre.

Note: Analgesic prescribing costs were a little under £500 million in 2010 in England. However, this total excludes the adjuvant analgesic use of medicines such as Pregabalin (which is classified as an antiepileptic) and pain related antidepressant prescribing.

It is not possible at present to determine accurately the number of people in the UK who are living with persistent pain who could benefit significantly from better treatment. But on the basis of studies such as those referred to above, they probably number at least one million at any one time. If it were assumed (as the available evidence suggests is so in the case of Fibromyalgia – Moore et al., 2010) that each individual involved could on average over the course of a year gain an extra 0.1 of a quality adjusted life year (QALY) from receiving improved pain care, this would imply a health gain potential of around 100,000 QALYs annually.

If the affordable value of an incremental QALY for NHS commissioners were to be conservatively set at £10,000 per annum, such figures suggest that the health service might reasonably consider investing up to £1 billion more annually (that is, in the order of one per cent of total NHS resources in England) on pain related treatments and services in future years, depending on the existence of suitably cost effective interventions. However, as noted in the introduction to this report, the

availability of such increased funding appears doubtful in the current economic climate. Realistically, the focus of care improvement is more likely to be on increasing the efficiency and effectiveness of existing resource use in primary and secondary care settings.

The following section considers aspects of how this might be achieved. However, a final point to add here is that continuing population ageing in the late stages of demographic and epidemiological transition is likely to go on increasing the prevalence of persistent pain in society. This is in part because of likely reductions in the effectiveness of pain inhibitory systems in older individuals (International Association for the Study of Pain, 2004). Finding cost effective ways of countering such trends through public health programmes and more accessible professional care for the mass of the population will become an increasingly important end, if health and social service costs are to be contained without increasing overall levels of distress. Extending and improving community pharmacy based care might offer a route towards such progress.

Box 4: The history of opioids, aspirin, and other analgesics

As described in the introduction, relieving pain has been a central goal of medicine throughout human history. Opium has been known since its cultivation over 5000 years ago by the Sumerians of Mesopotamia, and probably from long before then. The Sumerian ideograph representing the opium poppy meant 'joy plant'. This implies that opiates have always had mixed medicinal and recreational uses.

Perhaps because of such ambiguities, trade in opium flourished in Europe in the middle ages before seeming to disappear in the 1300s. But at the start of the seventeenth century opium was being purchased in India, and transported back to England. An apothecary, Thomas Sydenham, subsequently introduced a mixture of opium, sherry and herbs known as Sydenham's Laudanum, which became a popular remedy for a wide range of ailments .

The principal active ingredient of opium, morphine (the other is codeine), was first isolated at the start of the 1800s. It became widely available in Victorian Britain, where opioids were often more affordable than alcohol. Heroin (diamorphine) was synthesised towards the end of the nineteenth century, and was extensively marketed for medicinal use. Yet as the twentieth century progressed concerns about the addictiveness and harmful social and allied consequences of opiate use increased, and the legal availability of such drugs was curtailed. This was in part because of welfare concerns, and perhaps also because of a perceived need for enhanced social control.

In recent decades medically sanctioned opioid use has risen in the UK and other settings, along with trends like a rise in per capita alcohol consumption to levels last seen in Britain at the end of the 1900s. There

may be additional health outcome related benefits to be derived from further improving access to low dose opioids, as well as from enhancing severe pain treatment for those sections of the population currently least likely to receive it. Yet opioids remain from a regulatory perspective ambiguous – see main text. They are associated with abuse and addiction, particularly in socially disadvantaged groups and inadequately supported individuals, while also being in many circumstances the most effective drugs available for relieving pain related suffering (Rosenblum et al., 2008).

Aspirin, the first non-opioid analgesic to be discovered, has been through similar fluctuations in its popularity. Salicin, the active ingredient of Willow bark, was modified in 1897 to produce acetylsalicylic acid. This proved less irritating than earlier salicylate based analgesic medicines. In the first half of the 20th century aspirin's usage grew. But from the 1950s onwards it decreased, following the release of novel analgesics such as paracetamol and ibuprofen. However, the re-emergence of aspirin as a cardio-protective and as today a potential anti-cancer agent has meant that it remains one of the most widely used drugs in the world (Fuster & Sweeny, 2011), despite recurrent concerns about its relative and absolute safety.

The more recent development of NSAIDs has also been controversial. It would be inappropriate to describe their detailed history here. But perhaps the most important point to stress is that all medicines, analgesic or otherwise, exist as social objects as well as chemical entities. They can bring wealth and power to those who provide and regulate them, as well as relief to those able to take them effectively and harm to the less fortunate or ill-advised. Their biomedical properties are of course important. But it is the way in which medicines are used by communities and individuals which often serves as the ultimate determinate of their safety and value.

Treating pain

As described in Box 4, analgesic medicines have a long history. Yet the advent of specialised pain management services was very recent. In the case of adults their mainstream development commenced in the 1980s when anaesthetists started to organise acute pain services (Carr and Goudas, 1999).

In 1986 the World Health Organisation (WHO) launched the analgesic ladder, a framework initially designed to help clinicians to develop treatment plans for cancer pain. It has served as a catalyst for increasing awareness of the importance of treating pain in cancer patients (Vargas-Schaffer, 2010), and has also become a guide for treating other types of pain. The WHO analgesic ladder (Figure 8) is based on five simple recommendations regarding use of analgesics:

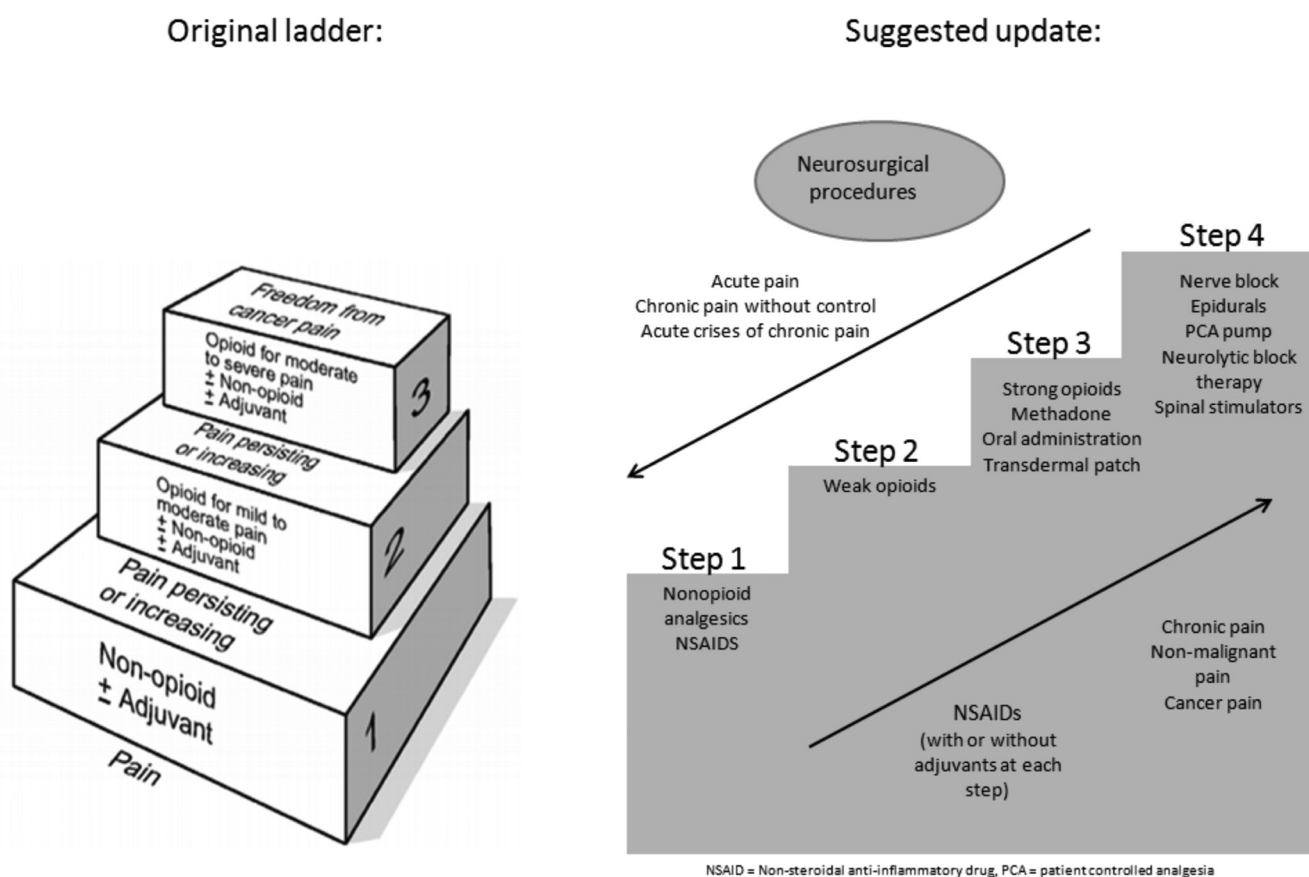
1. Oral administration should be used wherever possible.
2. Analgesics should be given at regular intervals to relieve pain adequately.
3. Analgesics should be prescribed according to pain intensity and evaluated by a scale of intensity of pain.
4. Dosing of analgesics should be adapted to the individual.

5. Analgesics should be prescribed with a constant concern for detail.

It has been claimed that the appropriate application of the ladder leads to effective pain control in 70-80 per cent of cancer patients (Kanpolat, 2007). Conventional pain management approaches start at the bottom of the ladder with medicines such as paracetamol or an NSAID and work up towards progressively stronger opioid and other drug combinations until the pain is satisfactorily controlled. It is recommended that two products belonging to the same drug category should not be used concurrently and it allows for the possibility of adding adjuvant medicines such as steroids, antidepressants or anticonvulsants for the treatment of neuropathic pain. Tricyclic antidepressants, for instance, can help moderate the transmission of pain signals up the spinal column.

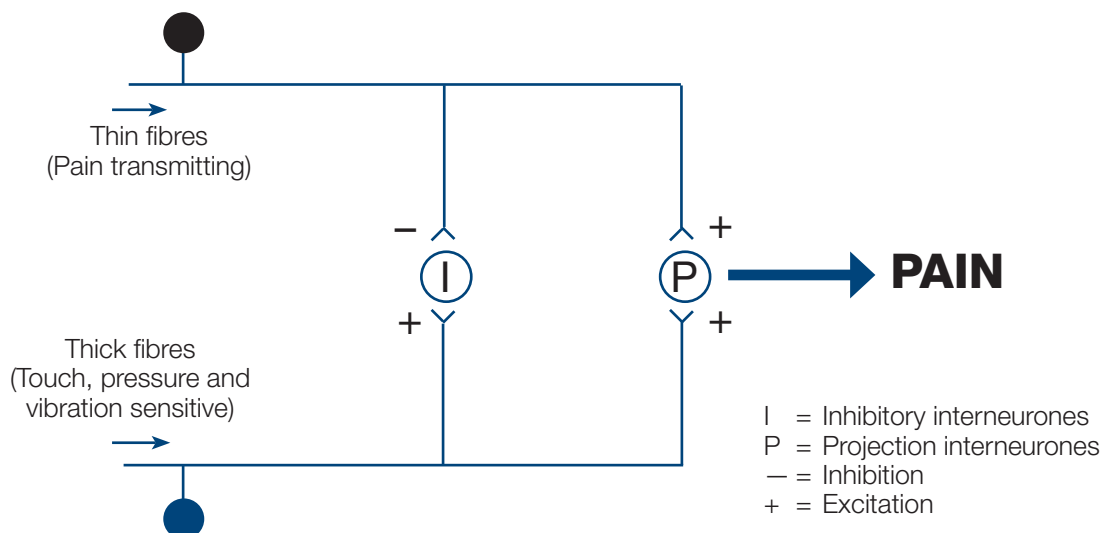
However, valuable though its use has proven the WHO ladder has been subject to growing criticism in recent years. There have been several proposals for modifications, including removing the second ('weak' opioid) step and adapting the scale to address more effectively other types of pain, such as acute and persistent non-cancer pain. Some commentators have also argued that the step-by-step process lacks urgency and is inefficient in the context of controlling intense pain. There have been proposals for a fast-track option

Figure 8. The WHO analgesic ladder and a suggested update which can be used in either direction and incorporates analgesic options such as spinal stimulators and transdermal patches.



Source: WHO and Vargas-Schaffer (2010).

Figure 9. The Gate Control Theory of pain.



Source: Melzack and Wall (1965).

Note: Excitation of the thin fibres reduces activity in pain inhibition pathways whilst excitation of the thick fibres enhances inhibition.

for use in the acute context where obtaining rapid relief is a priority, starting at level three and subsequently working down to the lowest interventional level at which acceptable pain control can be maintained.

Other suggested revisions include the integration of additional steps involving non-pharmacological interventions such as CBT (see below) or deep brain and spinal cord stimulation, and the use of additional medicines and/or drug administration routes such as, say, subcutaneous morphine or the use of transdermal fentanyl patches which did not exist when the ladder was first designed (Vargas-Schaffer, 2010).

Table 2 provides additional information on the wide range of medicines now available for controlling different forms of pain. It would be beyond the scope of this brief report to discuss the pharmacological and related properties of particular drugs in further detail here. But two general points are worth emphasising. The first is that it is difficult to predict how individual people with persistent pain will respond to any given medicine. In broad terms a rule of thirds appears to exist – a third of apparently suitable patients can be expected to respond well to new medication, a third will gain some benefit and a third will enjoy little or no improvement (Knaggs, 2011).

The dogmatic application of beliefs such as, for instance, opioids are always ineffective in the treatment of neuropathic pain should hence be avoided. The latter assumption is not in fact true (Scadding, 2003). Although the use of this class of medicines remains controversial (particularly in the US context – see Dhallaet al., 2011), patient and public interests arguably demand pragmatic and flexible therapeutic strategies aimed primarily at achieving good pain relief in a timely manner, whilst at the same time managing risks in informed and commensurate ways. There is evidence that currently the performance of the NHS in contexts ranging from post-surgical care to enabling people

living in significant pain promptly to access specialist medical and pharmaceutical care often seems to fall short of what might reasonably be expected, and that pain related outcomes in this country may have fallen below levels achieved in other European nations like France (Keogh, 2011).

A second general point to highlight here is that theoretical debate about the nature of pain has been taking place for literally hundreds of years. For example, the 'specificity theory' suggested that pain is experienced via a sensory apparatus independent of touch and other senses. The proponents of the 'intensive' theory, by contrast, speculated that pain can be generated by any sensory stimulus providing it is intense enough. However, the conceptual framework normally considered the most appropriate today stems from the 'gate control theory' originally postulated by Ronald Melzack and Patrick Wall in 1965 (Melzack & Wall, 1965).

Its key tenants are outlined diagrammatically in Figure 9. Gate control theory proposes that physical pain is not a direct result of the activation of individual pain receptors/neurons, but rather that pain perception is modulated by interaction between different forms of neuron. Melzack and Wall argued that two types of neuronal fibre – termed thin (pain transmitting) and thick (touch, pressure and vibration sensitive) – have balancing roles in the pain signal processing pathway. Specifically, excitation of the thin fibres reduces the activity inhibitory pathways, whilst thick fibre excitation enhances inhibition.

In practical terms this explains why actions such as rubbing an insulted area such as a stubbed toe reduces the level of experienced pain, and in part why massage used as an alternative therapy may have beneficial effects. Beyond this, the dissemination and further development of gate control theory enhanced the recognition that cognition, behaviour and socialisation play vital roles in the experience of pain, and led

Table 2. The main types of analgesic medicine

Class of drug	Examples and actions
Paracetamol	Also known as acetaminophen in the US, this is generally the first step in the pharmacological treatment of pain. The exact mechanism of action is unknown, but it appears to involve central inhibition of prostaglandin synthesis. This differentiates paracetamol from the NSAIDs (see below). There are limited side-effects, although repeated supra-therapeutic doses can be fatal (Craig, Bates et al. 2011).
NSAIDs	Non-steroidal anti-inflammatory drugs (NSAIDs), which include ibuprofen and diclofenac, work peripherally to inhibit the production of cyclooxygenase enzymes. This in turn limits prostaglandin production and results in anti-hyperalgesic (reduction in sensitivity to pain) and anti-allodynic (reduction in sensitivity to non-painful stimuli) effects. The majority of NSAIDs inhibit both COX-1 and COX-2 in ratios which differ from drug to drug. They show excellent control over acute pain which has an inflammatory or prostaglandin-related element such as post-operative pain, headache or period pain. They have no effect on neuropathic pain and are associated with gastrointestinal (GI) side effects ranging from dyspepsia (indigestion) to serious ulcer bleeds. Their use may also cause vascular disease related complications.
Coxibs	These COX-2 selective drugs, which include etoricoxib and celecoxib, were developed with the aim of reducing the GI side effects associated with NSAIDs. However, they were found to produce cardiovascular, renal and hematological side effects which in some circumstances outweigh their advantages, and two have been withdrawn from the market. Valdecoxib is no longer available because of the numbers of cardiovascular events in post-operative cardiac patients (McGettigan and Henry 2011) and Stevens Johnson syndrome. Rofecoxib was withdrawn due to increased cardiovascular events and stroke in patients who took it long term (Karha and Topol 2004).
Opioids	Opioids, including morphine and codeine, are generally reserved for moderate-to-severe pain, particularly nociceptive, cancer and post-operative pain and neuropathic pain in some situations. Opioids work by binding to widely distributed opioid receptors (generally the mu subtype). Activating relevant pre-synaptic receptors inhibits the release of excitatory neurotransmitters like glutamate and substance P. Post-synaptic opioid receptor binding decreases the probability generating pain related action potentials and so reduces feelings of pain. Side effects can include nausea and vomiting, dry mouth, constipation, miosis (pupil constriction), somnolence (drowsiness) and respiratory depression. Drugs such as morphine can also negatively affect dreaming. Acquired tolerance (decreased opioid receptor sensitivity and expression), opioid-induced hyperalgesia (where patients feel more pain due to opioid induced neurophysiological changes) and opioid dependence may also limit prescribing options (see main text).
Antidepressants	Antidepressants can be termed analgesic adjuvants, because although pain relief is not the main function of these drug they can usefully augment its treatment. Their analgesic effect is independent of their antidepressant function and involves several mechanisms. Tricyclic antidepressants such as amitriptyline inhibit the reuptake of noradrenaline and serotonin at synapses. They have a proven analgesic effect in a number of neuropathies, including fibromyalgia and diabetic neuropathy. Serotonin selective reuptake inhibitors (SSRI) and mixed serotonin and norepinephrine reuptake inhibitors (SNRIs) inhibit the reuptake of these neurotransmitters in the synaptic cleft in the dorsal horn of the spinal cord. This leads to an increase in their concentration, intensifying inhibitory action potentials in the descending pain pathways. The SNRI duloxetine is recommended by NICE as the first-line therapy for the management of painful diabetic neuropathy.
Anticonvulsants	Anti-convulsants also have an established adjuvant role in the treatment of persistent neuropathic pain in contexts such as post-herpetic neuralgia and trigeminal neuralgia. These drugs inhibit neuronal excitation and stabilise nerve membranes via ion channel blockade in the CNS, specifically the dorsal horn of the spinal cord. Gabapentin and pregabalin (which recently became the first drug approved by the US Food and Drug Administration specifically for the treatment of fibromyalgia) interact with voltage gated calcium channels. Both have been shown to successfully treat neuropathic pain. Current NICE guidelines indicate that pregabalin is the first-line treatment for neuropathic pain, but concerns about its costs compared to generic gabapentin have recently prompted NICE to initiate a consultation phase about revising its clinical advice. Adapted guidelines were due to be published in December 2011, although this has been deferred.
Topical analgesics	Topical lidocaine, which produces an analgesic effect by stabilising neuronal membranes and down-regulating neuronal sodium channels in order to reduce signal conduction, has recently been accepted for use in patients with post-herpetic neuralgia by the Scottish Medicines Consortium (SMC). Similarly, topical capsaicin has been shown to be useful in reducing pain in post-herpetic neuralgia and diabetic neuropathy, and a patch has been approved by the SMC. Capsaicin is the active ingredient in chillies and an agonist of the TRPV1 receptor, a heat activated ion channel. Continued activation of these receptors causes the depletion of substance P, a neurotransmitter involved in pain sensation.

psychologists to develop treatments designed to alter the perception and experience of persistent pain.

The resultant techniques, termed self-regulatory approaches, can help individuals to develop the skills necessary to become active participants in their own care, and avoid undue reliance on pharmaceutical therapies alone. These include biofeedback based interventions, relaxation training, hypnotherapy and mindfulness (Kerns et al., 2011). They are discussed further below, after a consideration of pain management at the population or 'public health' level and the challenges to be overcome in relation to pain assessment.

Pain as a public health challenge

Viewed appropriately, the problem of inadequately managed pain represents not only a discrete public health challenge which is comparable in magnitude and social impact to issues such as obesity in childhood or mental health problems such as depression, but which is also much more intimately linked to phenomena such as social class related inequalities in health than is commonly understood. Cost effective measures aimed at decreasing the incidence, duration and prevalence of persistent pain states through effective primary, secondary and tertiary prevention have a significant potential to reduce the economic and social burden associated with not only pain itself, but other distress and harm related factors. Examples of the ways in which this could be achieved include:

- the organisation of public and professional education programmes that raise awareness of chronic pain risk factors, and support the early identification of maladaptive pain;
- programmes designed to prevent the occurrence of painful conditions, such as encouraging shingles/ Herpes Zoster vaccination in the population aged over 50 or 60 years and educating more people about safe lifting techniques and allied fitness related topics. The latter could complement communication programmes on avoiding and managing conditions commonly associated with long term pain, such as lower back pain;
- developing and implementing appropriate pain management policies in hospitals and community health service organisations, to address problems like poor quality post-operative pain management;
- assessing the prevalence of persistent pain in local populations, and facilitating the provision of appropriately accessible specialist pain services in underserved areas; and
- enhancing NHS and other health work force skills relevant to managing pain efficiently in the primary care setting, in order to improve the early stage treatment of both uncomplicated acute pain and pain which could or has already become chronic.

In this last context, the potential for community pharmacy to contribute more effectively to pain management is discussed towards the end of this report. With regard to hospital and other institutional care, inadequate and untimely treatment of acute pain can as already described lead to the development of persistent pain states. Any acute pain episode should be viewed as having the potential to initiate a persistent neurological and behavioural event cascade which could have severe consequences for the affected patient. There is a window of time between acute and persistent pain states where it may be possible to apply appropriate diagnostic and treatment strategies to prevent peripheral and/or central sensitisation and other pathophysiological changes involved in the progression from acute to persistent pain. The key message is that adequately treating acute pain can prevent persistent pain, and that serious failures to take such opportunities should be seen as a form of professional negligence.

Relatively recent evidence indicates that only a third of hospitals in European nations offer specialised acute pain services, and that over half of anaesthetists are dissatisfied with postoperative pain management on surgical wards (Bandolier, 2003; Kehlet et al., 2006). The first step in reducing the incidence of persistent post operative pain is to identify those at risk. Important predictors include the presence of pre-operative pain, high reported anxiety and/or fear of surgery, obesity, age, genetic predisposition (Box 5) and patient and doctor expectations regarding the level of pain after surgery. Once at-risk patients have been identified, multimodal analgesia techniques can be employed to protect against sub-optimal outcomes.

There is some evidence that aggressive early pain relief can prevent some of the acute neuroplastic responses that follow tissue injury. However, there have been mixed reports regarding the effectiveness of pre-emptive and preventive analgesia (Kehlet et al., 2006). In this context it has, for instance, been hypothesised that central blockade of COX-2 (an enzyme involved in inflammatory pain) would lead to a reduction in prostaglandin synthesis and consequently a reduction in the likelihood of central sensitisation and resultant hyperalgesia (Langford & Mehta, 2006). Altering surgical techniques to minimise damage to major nerves may also limit the neuropathic pain component of persistent post-surgical pain.

There are a number of co-morbidities associated with persistent pain states. Illustrations include diabetes, cancer, HIV, obesity and depression. Increasing co-morbid disease incidence results in a concurrent rise in the number of people suffering pain (Canadian Pain Society, 2010a). Hence further improving HIV and cancer diagnosis and treatment could reduce the number of people with persistent pain conditions. Similarly, if investing in public health programmes were to reduce the incidence of obesity and diabetes, then the numbers of people affected by diabetic neuropathies should decline. Diabetic neuropathy is

Box 5: The Genetics of Pain

The variability seen in characteristics such as pain tolerance and individual propensities to develop persistent pain can to a degree be explained by genetics. The fact that a number of pain syndromes have a hereditary element (that is, they run in families) suggests a genetic basis for pain perception. Genetic factors affect this last by influencing the transmission of pain signals. They may also affect the survival of neurones, and be responsible for personal and gender related differences in pain perception, tolerance and analgesic responses.

SCN9A is an example of a single gene involved in three pain syndromes. It codes for the voltage-gated sodium channel $Na_v1.7$ and plays a vital role in pain perception. One of the diseases with which it is associated is 'channelopathy associated insensitivity to pain syndrome'. Sufferers feel no pain, and are at high risk of accidental harm as a result. (Recent research also suggests a role for $Na_v1.7$ in contexts such as diabetic neuropathy.) The other two diseases known to be associated with *SCN9A* are disorders of increased pain sensitivity. Both paroxysmal extreme pain disorder and primary erythromelalgia are caused by activating mutations in the gene sequence (Tremblay & Hamet, 2010).

A number of genetic variants have been shown to modulate the generation, transmission and processing of nociceptive information, although unlike the mutations discussed above they tend to have only a modest impact on pain phenotype. An illustration of this is the gene encoding the capsaicin receptor, *TRPV1*, which is related to a significantly reduced nerve-lesion induced heat and pinprick hyperalgesia. This is a common trait in neuropathic pain sufferers (Binder et al., 2011). Another gene known to be associated with the development of persistent neuropathic pain following mastectomy is *CACNG2*. This codes for a subunit of neuronal voltage-gated calcium channels, and so affects trafficking

of glutamate receptors to the neuronal membrane and modulation of signal transmission across the ion channel connected to glutamate receptors (Nissenbaum et al., 2010).

As well as affecting responses to pain signals, genetic variations also influence the effects of analgesic drugs. For example, opioid related effectiveness, tolerance and susceptibility to addiction all have a genetic component. The genes involved tend to be those that code for receptors, such as *OPMR1* which controls μ -opioid receptor expression, and those involved with drug metabolism, such as *CYP2D6*.

People with two normal copies of the latter have full enzyme activity and are known as extensive codeine metabolisers. People with one functional and one non-functioning copy are intermediate metabolisers. Those with no functionally active copies of *CYP2D6* have minimal enzyme activity. They are poor codeine metabolisers, and receive little benefit or no from this drug (Australian and New Zealand College of Anaesthetists and Faculty of Pain, 2010). Approaching 10 per cent of the UK population falls into this last category. A number of polymorphisms have also been found in *PTGS2*, which codes for the COX-2 enzyme. They may explain inter-individual variability in experienced acute pain levels and the analgesic activity of some coxibs and NSAIDs (Australian and New Zealand College of Anaesthetists and Faculty of Pain, 2010).

As yet, applied genetics has only a modest role in improving pain management. But it will in time lead to the development of more personalised medicine, and novel treatment techniques such as gene therapy. The ability to genotype someone for a 'pain susceptibility' gene may in time prove to be of significant social benefit, not least through helping to remove the stigma that is sometimes experienced by people afflicted by persistent pain.

currently believed to be responsible for approaching one in every twenty persistent pain cases (Pain Proposal Committee, 2011).

Psychiatric co-morbidities are also common in patients suffering from persistent pain. It has been claimed that four out of every five persistent pain patients suffer from depression, although in practice the presence of pain may obscure associated mental health problems. Optimisation of depression treatment could aid the diagnosis and treatment of persistent pain and decrease its severity (Chan et al., 2009). Similarly, anxiety and persistent pain are linked, not least in the sense that both can be seen as forms of nervous system hyper-arousal that require de-escalation. On occasions anxiety about pain can exacerbate the pain experience, and lead on to a pain-anxiety vicious cycle. From a public health perspective, helping patients and professionals better to understand this relationship should help improve outcomes.

Other public health initiatives aimed at reducing the occurrence of not only chronic diseases but also societal objectives like curbing rates of injury associated with accidents and violence or service goals such as improving access to dental care could also decrease persistent pain prevalence (Institute of Medicine, 2011).

A comprehensive public health approach ought to involve a wide range of community leaders and representatives. Such initiatives could, for instance, seek to promote wider public appreciation of facts like exercises which strengthen the back or trunk and increase cardiovascular fitness can reduce low back pain incidence (Linton & van Tulder, 2001). Likewise in relation to osteoarthritis, interventions that successfully reduce the occurrence of weight related problems could also help protect joints and tendons from avoidable harm.

Pain assessment

The success of any clinical intervention intended to control persistent pain is in large part dependent on appropriate patient evaluation and selection, that adequately takes into account each individual's unique situation and needs (Nocom et al., 2009). Notwithstanding recent developments in areas such as the functional imaging of nervous system activity, there are as yet no 'objective' external measures of pain. Its assessment – as with psychiatric states such as depression – must therefore rely on patients' reports.

Some medical and other professionals may in the past have dismissed the latter as being 'inherently subjective', and in so doing risked becoming insensitive to the concrete realities of their patients' experiences. In fact, well designed instruments can provide relatively robust ways of assessing the latter (Box 6).

Recognition of the reality that unmanaged pain can compromise health has led to increasing numbers of medical associations and accreditation bodies to take the view that pain severity should be regarded as a 'fifth vital sign', along with blood pressure, temperature, heart rate and respiration rate (Rosenblum et al., 2008). Such observations again imply that failures to assess pain adequately in both acute and long term care settings are in future increasingly likely to be regarded as indicators of unacceptably poor practice.

In acute situations the most common type of pain is nociceptive, which can be divided into:

- somatic – sharp, hot, stinging pain, which is generally well localised and is associated with local and surrounding tenderness
- visceral – dull, cramping or colicky pain that is often poorly localised (and located deeper in the body). It may be associated with local tenderness and/or referred pain, and with symptoms such as nausea, sweating and cardiovascular changes.

However, neuropathic pain is also encountered in acute settings. The features in a patient history that may point towards neuropathic pain include:

- burning, shooting or stabbing sensations
- spontaneous pain onset
- the presence of hyperalgesia, allodynia or dysaesthesia (that is, unusual levels of sensitivity to stimuli that may or may not normally be painful, and reports of abnormal spontaneous or evoked sensations such as a feeling of acid burning under one's skin)
- autonomic nervous system driven changes such as changes in tissue colour, temperature and sweating

Acute pain assessments ought to be repeated at appropriate intervals using a suitable assessment tool to evaluate pain intensity, functional impact and treatment side effects (Australian and New Zealand College of Anaesthetists and Faculty of Pain, 2010). A

Box 6: Pain assessment resources

Links to internet sites containing information and assessment instruments of use in relation to pain management are provided at the end of this report. In addition, health professionals such as community pharmacists can access resources such as the Centre for Pharmacy Postgraduate Education's (CPPE's) Focal Point Learning Programme on pain (see www.cppe.ac.uk).

In association with the preparation of this report, the UCL School of Pharmacy has produced a semi-structured discussion guide for use by community pharmacists and pharmacy service users entitled 'Talking About Pain'. This does not seek to duplicate the material available from other sources. It is intended to support informal consultations about pain related issues in an easy to use but nevertheless evidence based manner. It is available at the UCL School of Pharmacy website and via Dr Sarah Carter of the UK Clinical Pharmacy Association (www.ukcpa.net).

suitable assessment instrument is one that is relevant to and appropriate for the person concerned, taking into account their age, race, socioeconomic status, emotional condition and mental and physical health. It should address variables such as the location of their pain and its quality and sensory characteristics, together with its intensity, duration, variability, predictability and the existence of any aggravating and alleviating factors. It should also be used as early in the care process as possible (ICSI, 2007).

A number of scales are available for use by patients/ members of the public independently, or in collaboration with health professionals like doctors, nurses and pharmacists. Categorical scales use words to describe the magnitude of pain: the most common example is the verbal descriptor scale (VDS). For comparison over time, terms such as mild, severe and agonising can be converted to numeric scales. These scales can relatively easily be employed by or with members of virtually any patient group, although their simple linguistic structure normally makes it relatively difficult to detect small changes in experienced pain.

Numerical rating scales (NRS) typically enable patients to rate their pain intensity on a scale of zero to ten, where zero represents 'no pain' and ten represents 'worst pain imaginable'. Such a scale can also be used to measure pain relief with zero representing 'no relief' and ten representing 'complete relief'. Visual analogue scales (VAS) are also commonly used in pain research and evaluation. They characteristically require those using them to indicate on a (say) 10 centimetre line where their pain falls between two verbal descriptors like 'no pain' and 'worst pain'. This is then converted into a numerical score by measuring the distance between the beginning of the scale and the point marked.

When assessing persistent non-cancer pain it is often necessary to use something like the Change Pain Scale, which uses a holistic approach that takes into account patients' expectations regarding pain relief and quality of life. It may also be necessary to use a pain diagnostic aid to determine if there are neuropathic components to persistent pains. Those available include the *Leeds Assessment of Neuropathic Symptoms and Signs* (LANSS), the DN4, and PainDETECT.

Pain assessment is particularly difficult in instances where communication problems exist. Those with poor English and people with age related and other mental and cognitive limitations typify the groups most likely to have limited communication skills. Children are also likely to have special requirements in this area. The behavioural assessment scales available for them include the modified Faces, Legs, Activity, Cry and Consolability (FLACC) scale (Australian and New Zealand College of Anaesthetists and Faculty of Pain, 2010).

In children, as in adults, pain assessments are vital for optimal pain management. They should involve a clinical interview with the child and/or their parent/carer as well as a physical assessment, and the use of an age and context appropriate pain intensity measurement tool. Although self report is considered the best measure of pain in adults it is not always possible in children as their understanding of pain and their ability to describe it changes with age.

In neonates changes in physiological parameters such as respiratory rate and blood pressure that are associated with procedural interventions can be taken to indicate the presence of pain. However, monitoring facial responses such as 'horizontal mouth stretch' and 'taut tongue' have been found to be more reliable than physiological measures for evaluating pain in neonatal intensive care (Stevens et al., 2007).

Ten facial actions have been included in the *Neonatal Facial Coding Scale* (NFCS). Other neonatal pain assessment tools available for use include PIPP, COMFORT and CRIES, although not all have been rigorously evaluated (Australian and New Zealand College of Anaesthetists and Faculty of Pain, 2010). Self-reporting in children is normally possible by age four but will depend on cognitive and emotional maturity. Examples of established self-reporting tools include *Pieces of Hurt*, the *Faces Pain Scale-Revised* and VAS to be used in 3-4 year olds, 4-12 year olds and those over 8 years old respectively.

In the case of cognitively impaired adults verbal and numerical rating scales can be used, provided that appropriate assistance is available. People who lack verbal and numeracy skills, perhaps due to an event like a stroke, may be able to respond to a suitably adapted pictorial rating scale. Support from a speech therapist or a psychologist may help with self-reporting (Royal College of Physicians et al., 2007).

Psychological and other non-drug interventions

Normally, psychological and other non-drug interventions are considered after orthodox pharmaceutically based analgesic interventions have failed to provide adequate relief and/or what might originally have been regarded as a self limiting acute episode has failed to remit. This is because at such points the focus of treatment changes from that of temporarily alleviating pain to learning how to manage and live with it, in the hope that the problem will in time become more manageable and eventually resolve. Although in future the first line use of non-drug treatments might desirably increase, this overall pattern seems likely to remain.

Psychological treatments used in pain relief are intended to influence processes thought to underlie pain perception and the distress and disability that painful states cause. They reflect a biopsychosocial approach to pain and can be characterised as either theoretically based or specific practical techniques. The most common of the former include operant conditioning and cognitive behavioural therapy (CBT). Examples of specific techniques used include relaxation, hypnosis and cognitive therapy (Turk et al., 2011). Meta-analyses have confirmed that psychological approaches have positive impacts on moderating pain intensity, on improving functional performance and quality of life, and on reducing depression (Williams & Morley, 2009; Institute of Medicine, 2011).

The majority of the modern pain management community recognises the benefits of multidimensional, multimodal and interdisciplinary strategies for the relief of persistent pain. Psychological and linked behavioural interventions are now recognised as effective and important components of persistent pain management.

As discussed previously, self-regulatory approaches rest on an understanding that habitual states of mind coupled with other factors, including expectations and beliefs, can contribute to the development and exacerbation of persistent physical pain (and vice versa). They employ appreciations of such mind-body connections to increase an individual's sense of control over emotions, thoughts and sensitivity that are commonly believed to be out of personal, volitional, control (Kerns et al., 2011).

Examples of self-regulatory approaches include (McCracken et al., 2007):

- *Biofeedback*
 - » Individuals are provided with 'real-time' feedback about a variety of physiological processes in order to develop an awareness of change relationships
 - » This furnishes them with opportunities to learn how to exert voluntary control over their bodily reactions and states.

- » Biofeedback techniques have been shown to be effective in controlling conditions such as migraine and tension-type headaches for periods of a year or more.
- *Relaxation*
 - » Relaxation support techniques are often used concurrently with biofeedback training and other treatment regimes.
 - » They involve identifying states of tension within the mind and body and the subsequent use of methods such as diaphragmatic breathing, progressive muscle relaxation and visualisation to bring them under greater control.
 - » Learning relaxation techniques educates individuals about the links between emotional and physiological stress and distress, and enables them to develop improved self-control abilities that directly affect their experience of pain
 - » They have been shown to be of value in the management of migraine, musculoskeletal and low-back pain.
- *Hypnotherapy*
 - » Hypnotherapy is closely related to relaxation therapy but involves individuals entering an altered state of awareness, guided by suggestions from a hypnotherapist.
 - » Hypnotherapy can be used to focus a patient's attention in ways that can change their subjective experience of pain.
- *Mindfulness*
 - » Mindfulness is a concept rooted in the principles of Theravada Buddhism. It involves fostering a calm and rational awareness of one's own body and the realities of the present
 - » It can counter the effects of narrowed awareness and the emotional and behavioural impacts of distressing experiences.
 - » There are similarities with relaxation and hypnotherapy based interventions, although mindfulness emphasises attaining stress reduction through increased focus on phenomenon occurring in the moment, without reference to the past or future.
 - » States of mindfulness have been significantly linked with pain and pain-related distress reduction.

Behavioural therapies are based on the fact that behaviours that are reinforced/rewarded tend to increase in frequency, while those that are punished or unrewarded decrease in frequency. As far as persistent pain management is concerned, targeted response patterns include excessive verbalisation of pain (such as grunting or sighing), frequent discussion about pain or discomfort, guarded or restricted movements, and selected facial expressions. These behaviours

are commonly reinforced by responses from family and friends such as sympathy, which although understandable can have the effect of trapping individuals in 'pain centred' mindsets and roles.

Operant behavioural therapy (OBT) attempts to reduce the pain related behaviours and reinforce 'healthy' behaviours (Kerns et al., 2011). There is evidence that it can be effective as a mono-therapy, as well as in combination with other forms of treatment (Smeets et al., 2009).

Acceptance of pain, without wishing to control or avoid it, has been linked to reductions in the intensity with which it is experienced, and the distress and disability caused (McCracken & Zhao-O'Brien, 2010). Acceptance and commitment therapy (ACT) emphasises the value of observing thoughts and feelings as they are, without trying to change them. One rationale for this is that although pain hurts, fruitless struggles to deny or control pain cause additional suffering.

Controlling negative thoughts, feelings and behaviours associated with experiencing pain may therefore benefit individuals (Kerns et al., 2011). A recent study indicates that patients receiving ACT for persistent pain remained in a substantially improved state three years after treatment completion, and that gains relative to a follow-up conducted three months after treatment completion were maintained (Vowles et al., 2011).

Perhaps the best known form of behavioural therapy for the treatment of persistent pain is cognitive behavioural therapy (CBT). This can help patients break the cycles of pain, fear, immobility and social withdrawal that lead to progressively worsening levels of experienced pain. There are three basic components to CBT for pain management:

1. A treatment rationale that helps people who are living in pain to understand better that thoughts and behaviours influence pain experience, and that individuals can play an effective role in controlling their own pain.
2. The development of coping skills such as progressive muscle relaxation, activity pacing and pleasant activity scheduling.
3. The application and maintenance of learned coping skills.

CBT has been shown to be effective in treating persistent pain problems when compared to waiting-list controls and alternative active treatments (Kerns et al., 2011). A recent Cochrane review found it to have a small to moderate effect on pain as measured immediately post-treatment, compared with no intervention (Williams & Morley, 2009). There may be opportunities to design computerised CBT (CCBT) programmes for persistent pain comparable to other initiatives such as the 'Beating the Blues' programme used in the context of depression (Spurgeon & Wright, 2010). This could enable large numbers of people to access CBT at low cost. One study showed that

an online persistent pain self-management program including modules in cognitive, behavioural, social and emotional regulation significantly reduced pain-severity, emotional burden, depression, anxiety and stress (Ruehlman et al., 2012).

Psychological therapies such as individual and group CBT are often delivered in the context of pain management programmes (PMPs) which are intended to enhance physical performance and help participants cope more effectively (Nurmikko et al., 1998). In 2007 the British Pain Society (BPS) published guidelines for PMPs in an attempt to promote greater consistency (The British Pain Society, 2007).

The inclusion of physical or rehabilitative therapy in some PMPs is based on the fact that physiotherapy can also reduce pain intensity and use of pain medication. In addition, physical conditioning/therapy programmes can be effective in reducing the number of sick absence days caused by conditions such as persistent back pain, when accompanied by CBT (Institute of Medicine, 2011). Appropriate services not only reduce pain directly, but also give patients the knowledge and skills to maintain their health and function which may help maintain psychological well-being (Chief Medical Officer, 2008).

The realisation that complementary physical and psychological approaches to the alleviation of pain can act synergistically led the authors of the National institute for Health and Clinical Excellence (NICE) guidelines on the treatment of low back pain to recommend a combined treatment programme (NICE, 2009). However, such treatments are not as yet widely provided.

Complementary medicine, including massage therapy, music therapy, acupuncture and yoga, is commonly used for the self-management of pain. In 2007 over 40 per cent of Americans with chronic pain or neuralgic conditions reportedly used complementary medicine of one sort or another (Institute of Medicine, 2011).

Other non-drug interventions include nerve stimulation, nerve ablation and neurosurgery. Such treatments can serve as a last resort for people who have not received relief from other forms of treatment. Spinal cord stimulation (SCS) was first reported in 1968, although it has only relatively recently been refined for clinical use. It is now thought that SCS activates pain inhibiting circuits in the spine, resulting in a pleasant numbing sensation (Nurmikko et al., 1998). Large studies indicate that SCS can deliver good long term outcomes (>50% pain reduction) in 50-60 per cent of cases treated. As a result of such trials, SCS has now been included in the NICE guidelines for the treatment of people with persistent neuropathic pain provided that they have had their pain for at least six months and have undergone an assessment and trial (NICE, 2011b).

Transcutaneous electrical nerve stimulators (TENS) work in a similar way, using electrical energy to activate spinal cord nerves. This competes with, and blocks,

pain signals. It can have a significant effect on multiple types of pain, particularly if used in conjunction with other treatment options (Chief Medical Officer, 2008).

Radiofrequency lesioning of the nerves or ganglion, a neuro-destructive technique using heat to produce controlled tissue destruction, is also frequently advocated. Pain transmission is said to be modulated without causing clinical signs of nerve damage. However, the pain relief gained is typically temporary due to nerve regeneration.

Finally, surgical therapies to reduce or remove persistent pain may be seen as overlapping with techniques such as spinal cord stimulation and spinal analgesic infusion pumps. However, they often involve invasive procedures such as spinal decompression, disc replacement, spinal fusion and joint replacement. Others types of surgical interventions include ablative surgeries, such as nerve section and cordotomy, which disrupt the flow of nociceptive pain signals.

Some surgical interventions that have pain reducing effects, such as hip replacement, are of robustly proven utility and cost effectiveness. But others are controversial. In the latter circumstances it seems prudent to regard surgery as a last resort, to be recommended only when other treatment options have failed (Institute of Medicine, 2011).

Adherence in medicines taking

Adherence, or the extent to which a patient takes medicines in a way precisely in line with his or her professionally agreed regimen, is often said to be as low as 50 per cent in the context of chronic disease treatment in countries such as the UK (Trueman et al., 2010). Although the consequences of this should not be exaggerated, there is evidence that sub-optimal medicines use imposes costs significantly in excess of the more visible problem of medicines wastage *per se*.

However, it could be argued that in the context of pain relief non-adherence should not be a matter of concern. This is because as pain is a subjective experience it may be thought that it is purely a matter of personal choice whether or not someone living with pain feels they need to use an analgesic drug or not.

There is a strong argument in favour of this view in cases of minor acute adaptive pain, such as that typically treated by over-the-counter purchased paracetamol, aspirin or NSAIDs. Indeed, minimising the 'unnecessary' use of such drugs may well be regarded as a positive end. However, in cases of more serious and/or persistent pain there is evidence that if individuals only take analgesic medicines at times when they feel they must this leads to poorer pain control than when such drugs are used in an appropriately planned, anticipatory, manner. At worst, failures to prescribe or use pain relieving medicines optimally can in these circumstances not only lead to needless personal distress in the short term, but serve to promote and extend episodes of maladaptive

pain. The occurrence of 'non-compliance' in these circumstances can be indicative of inadequate patient-professional communication and other forms of care and service failure.

In cases of persistent pain, adherence to medical treatments may be limited due to the complexity of medical regimens, drug side-effects, and a lack of the pharmaceutical and medical care support needed to manage the latter. The therapeutic outcomes achieved by persistent pain patients tend to be compromised by high rates of tolerability-related treatment discontinuation. It is hard to maintain a balance between pain relief and medication tolerability and patients often find themselves in an 'analgesic vicious cycle' whereby insufficient analgesia accompanied by acceptable levels of side effects leads to an increase in dose. Yet while this may provide sufficient analgesia, it may result in intolerable side effects and subsequent dose lowering.

In addition, opioid tolerance may lead to larger doses being required which may then result in an increased incidence of side effects leading to treatment discontinuation. Persistent pain patients are more likely to stop opioid treatment due to adverse effects rather than lack of analgesic efficacy, albeit that non-adherence may also be linked to treatment ineffectiveness. This can in part stem from physicians or other prescribers failing to differentiate between nociceptive pain, pain related to inflammatory conditions, neuropathic pain and pain where there is no clear stimulus or damage.

Such observations underline the importance of robust pain assessment approaches and regular monitoring of treatment effectiveness, although having said this making precise 'pain diagnoses' can be very challenging and the selection of effective treatment subject to high degrees of uncertainty. For example, one illustration of the complicating factors that can occur is that central-post stroke pain can start months or years after the initiating stroke or allied event. Also, persistent pain is often a mix of both nociceptive and neuropathic pain (Scadding, 2003). In a recent European study it was found that two-thirds of the neuropathic pain sufferers questioned were being prescribed NSAIDs, which are unlikely to have been effective (Gustorff et al., 2008).

In cases of pain with mixed aetiologies, combination therapies involving drugs with multiple mechanisms of action may be required. Such approaches can result in additive or synergistic analgesic effects, and/or an efficacy comparable to higher doses of single drugs but with a more favourable side effect profile. For example, in one placebo controlled trial a combination of morphine and gabapentin was found to provide better pain relief than each drug alone, although the net gain observed was relatively modest (Gilron et al., 2005). However, the use of multiple drugs may on occasions be accompanied by a higher incidence of drug-drug interactions, particularly in vulnerable populations.

Unfortunately, there are a minority of people for whom pharmacological interventions intended to relieve pain do not work, and where it may not be possible to satisfactorily explain their symptoms and underlying conditions. In the past such patients may sometimes have been dismissed as 'malingerers', or otherwise effectively ignored. A key message of 'pain campaigners' is that it is vital that they are not 'forgotten' in systems such as the NHS. Rather, they should be referred on to pain management specialists, who at the very least should be able to help them learn to accept and live with their pain with less distress than would otherwise be the case.

Pain in 21st Century Britain – Improving Outcomes

Access to effective pain management should, many commentators who have a good understanding of this field of medicine and pain's impacts on individuals and society believe, be regarded as a fundamental human right. This view can be regarded as analogous to the ethical position that civilised societies should not condone torture.

The great majority of health professionals working in the NHS wish to do their best to ensure the wellbeing of their patients. Yet despite this reality (and clear evidence of recent progress, such as the publication in Scotland in 2008 of the GRIPS Report and the English DoH's 2010 'Essence of Care' benchmark on pain – see below) many people with pain are not being as effectively treated as they could be.

One possible explanation for this could be that some healthcare professionals (along with a proportion of their patients) believe that pain reporting is essential for diagnosis and condition monitoring, and that only awkward individuals complain when they feel that their discomfort is not being adequately controlled (Brennan et al., 2007). The fact that as yet reducing the burdens imposed by persistent pain is not an agreed national priority in England may also have contributed to this situation (Pain Proposal Committee, 2011), as on occasions does the stigmatisation of people living with conditions such as pain and depression. In addition to addressing this issue, which is discussed further in Box 7, the types of policy measure and service improvement needed to further enhance access to effective pain management in England and improve outcomes include:

- raising via public health interventions overall public understanding of the causes of chronic pain, and how it can best be avoided or controlled by individuals and their families. Progress in this area should also be supported by the further involvement of employers and other community agencies such as local authorities;
- strengthening professional education;
- further national and international acceptance of the existence of maladaptive pain as a medical condition

in its own right, which is becoming identifiable by characteristic nervous system abnormalities in the spinal cord and elsewhere;

- the extended provision of specialist multi-disciplinary pain management services in underserved areas, coupled with measures that promote good access to all effective pharmaceutical and non-pharmaceutical treatments in appropriate combinations; and
- improved primary care provision, designed to make full use of existing mass access care providers/ gateways such as community pharmacies. Developing 'healthy living pharmacies' and allied community resources in ways which enable more people with or at risk of chronic pain to be identified as early as possible and treated promptly is arguably an essential part of any population level oriented, public health based, pain management strategy. Persistent pain interferes with everyday activities and social functions and undermines quality of life. Between half and two-thirds of sufferers say they are less able or unable to exercise, enjoy normal sleep, perform household chores, attend social activities, drive a car or walk. Perceptions that there is a low society-wide awareness of such consequences of chronic pain can increase feelings of social exclusion among those whose lives are affected by it.

There is evidence that people with persistent pain want confirmation that their pain is 'real' and to have good access to consistent and reliable information (Pain Proposal Committee, 2011). But at present some 40 per cent feel that their condition is inadequately managed, with half saying that their doctor does not view their pain as a problem (International Association for the Study of Pain, 2004). One in four people with moderate or severe persistent pain claim that their doctor never asks about their pain, does not think that they have a problem, or – if pain is discussed – spends too little time on it and does not know how to treat it.

This apparent lack of professional concern regarding persistent pain may in part be due to educational limitations. It has been pointed out that the undergraduate medicine curriculum involves an average of 13 hours of pain related content (Briggs et al., 2011). Pharmacy students have in the past received only eight hours. By contrast, veterinary science courses typically include 27 hours on animal pain management issues, while physiotherapists receive 37 hours relevant training.

Such deficiencies seem to have contributed to less than half of doctors reporting that they feel confident knowing what to do if a patient still complains of pain after initial treatment, and three-quarters requesting more training on persistent pain (Pain Proposal Committee, 2011). The communication of medical uncertainty can become an additional challenge for patients, by at times exacerbating their sense of stigma and leading them to believe that they are being 'written off as psychologically defective' (Canadian Pain Society, 2010b).

To combat this it has been suggested that pain management should become a core element of

Box 7: Pain and stigma

Stigma is perhaps most commonly thought of as a phenomenon that affects people with mental health problems such as schizophrenia or depression, and/ or disadvantages such as severe learning disabilities or major impairments of appearance. But it can also affect individuals who are living in pain. Stigma has been described as having three main dimensions – ignorance (lack of knowledge), prejudice (unfair judgement) and discrimination (whether or not people are socially excluded, or are otherwise unfairly treated in practice) (Thornicroft 2007).

Pain, like depression, is largely unseen and is often not fully explicable and as a consequence may be feared. Hence those living with it may on occasions be regarded as seeking to avoid their normal responsibilities and accused of 'skiving', or seen with varying degrees of hostility to be undermining others by not 'taking part' constructively. They may even sometimes come to judge themselves negatively, because of the limitations that chronic pain can impose on their daily lives and their self-perceived inability to contribute to the wellbeing of those around them.

Reducing the risk of stigmatisation consequently requires action at a variety of levels. Public health and professional education programmes on persistent pain and allied topics can, for example, reduce levels of ignorance, and so decrease the probability of individuals being exposed to unfair judgements and actions. At the same time improved personal and family level care can not only relieve experienced pain levels. It can in addition decrease the anxiety and distress of those around people who are in pain. It may also help patients not to be unduly critical of themselves, and to be more fully aware of their positive achievements and opportunities.

medical education standards and quality assurance mechanisms. Proponents of this view say that health care commissioners and providers ought to prioritise the provision of appropriate pain relief training for all health workers, particularly in primary care, and should emphasise the need for early recognition of the precursor stages of persistent pain (Phillips et al., 2008). To this end the British Pain Society, the Chronic Pain Policy Coalition (CPPC), the Royal College of Anaesthetists Faculty of Pain Medicine, the Patients Association and the Royal College of General Practitioners (RCGP) recently applied for funding to develop online educational material for all health workers who come into contact with patients who are in pain.

Effective policies also need to include a clear focus on the provision of robust information for patients, and an emphasis on the value of self-help strategies (Phillips et al., 2008). One example of good practice is that a little over ten years ago in Australia a television campaign was used to encourage people to stay active in spite of experiencing pain. This approach reportedly had a prolonged effect on sickness absence rates, as well as other areas such as reducing the risks of stigmatisation (Buchbinder et al., 2001).

Pain and employment

Remaining in work can contribute to both physical and mental health, and often improves individuals' quality of life and self-esteem (DWP, 2008). For communities it can have the added benefit of reducing pain-associated costs like those incurred because of the payment of sick benefits. Effective policies ought to emphasise the occupational-clinical interface, and help people who want to remain in employment to do so despite having to face challenges such as persistent pain (Phillips et al., 2008). Employers can play key roles in understanding and contributing to rehabilitation processes, and patients' return to work after periods of enforced absence (Chief Medical Officer, 2008).

Recognising persistent pain as a long term condition

The past decade has seen a worldwide shift in political as well as professional attitudes towards persistent pain. In addition to the Australian, Canadian and other international initiatives referred to earlier, an important symbolic illustration of this progress was that the US Congress named 2001-2010 as the 'decade of pain control and research' (Kerns et al., 2011).

In the UK, the Royal College of Anaesthetists established a Faculty of Pain Medicine in 2007 and the 2008 Chief Medical Officer for England's report highlighted the extent of chronic pain and its impact on individuals, families and the overall economy (Chief Medical Officer, 2008). The Welsh government has also published a commissioning strategy focused on persistent pain (NHS Wales, 2008).

Since then other key developments have included the establishment of a National Pain Audit by Dr Foster research and the BPS, and the publication in October 2010 by the Department of Health (DOH) of a new Essence of Care benchmark on pain (DOH, 2010). An important component of this last is ensuring that people have an 'ongoing, comprehensive assessment of their pain' by trained staff using evidence based tools. Persistent pain has also become a Royal College of General Practitioners clinical priority for 2011-2014. Together with the BPS, the CPPC, the Royal College of Anaesthetists Faculty of Pain Medicine and Patients Association, the RCGP recently put forward proposals on improving relevant service standards to the NHS' National Quality Board. The same organisations were also involved in the organisation of the National Pain Summit, held in London on the 22nd November 2011 (Chief Medical Officer, 2010).

One aspect of an increased awareness of the causes and harm associated with chronic pain has been a growing acceptance that maladaptive pain can usefully be understood as a discrete form of illness, independent of the conditions or events that may originally have precipitated it. For example, in Scotland the GRIPS (Getting Relevant Information on Pain Services) report (NHS Scotland, 2008) recommended

the formal national recognition of persistent pain as a clinical entity in its own right.

Proponents of this approach argue that it will further increase public and professional awareness of the problem, and will combat the neglect of pain associated with viewing pain as 'merely a symptom'. But not all participants in this debate accept such reasoning. Critics may, for instance, feel that it implicitly condones the insensitivity that may lead some practitioners to neglect the treatment of their patients' distress, regardless of how it is described. But it is nevertheless of note that the conventional definition of a disease requires the existence of an '*identifiable disorder of structure or function and not just a grouping of symptoms*'.

Modern neuroimaging studies have shown that persistent pain patients have altered brain and other nervous system structures and/or functioning. Although it remains uncertain as to the extent to which the changes observed are a normal adaptive response to continuous nociceptive input or are critically involved in causing persistent pain states (Tracey & Bushnell, 2009), such findings may be taken to favour the view that chronic pain can be regarded as a discrete medical condition.

However, whether or not persistent pain is designated as a long-term disease, what is certain is that, for substantial outcome improvements to be achieved, a 'joined-up' approach to care provision will be needed. Sufficient resources should be allocated to reducing the prevalence of pain and its immediate and longer term impacts (Phillips et al., 2008). But at the same time all those involved share responsibilities to help develop services which work cost effectively, to provide the greatest affordable relief to the largest possible number of people.

Controlling pain and drug misuse

From a public policy standpoint a key issue related to controlling pain involves balancing fundamental personal rights to timely access to effective pain relief with guarding against the abuse potential and possible social as well as patient safety related costs of using opioid and other analgesics. Opioids can be valuable in the treatment of most if not all types of persistent pain, even if more often than not complete pain relief is rarely achieved through drug use alone and they are in large part prescribed to reduce pain intensity in order to enable active engagement with rehabilitative activity and psychological adjustment.

There is evidence that appropriate long-term opioid therapy can help patients have an improved quality of life, use health services more economically and improve productivity (Rosenblum et al., 2008). But against this inappropriately used opioid containing medicines can cause significant harm. It has recently been reported that in the US deaths involving opioid analgesics increased from 4041 in 1999 to 14,459 in 2007 (Dhalla et al., 2011). There has also been an increased

use of prescribed opioid medicines usage in Britain, albeit there appears to be proportionately much less associated harm (The National Treatment Agency for Substance Abuse, 2011).

While some health professionals wish to curb opioid use in the UK countries, others are concerned that this would be counter-productive in terms of health outcome improvement. It has been reported internationally that approaching a third of primary care physicians and one in six pain specialists say they prescribe opioids less often than they think appropriate because of concerns about regulatory repercussions (International Association for the Study of Pain, 2004).

Striking a balance between such concerns is always likely to be problematic. Optimising the cost benefit ratio of any form of potentially addictive and/or harmful medicinal drug will depend on appropriate patient selection and the careful monitoring of their use in individual patients and given communities. Patients with a history of substance misuse or with a co-morbid psychiatric diagnosis are probably more likely to develop problems with opioid use than others, as are members of any relatively disadvantaged community. However, such individuals are also likely to be most at risk of receiving inadequate pain relief, particularly in societies like that of the United States.

There are various management strategies that can be put in place to minimise the risk of opioid misuse, including the registration of patients on high dosage and/or long term therapy. But the insensitive employment of potentially stigmatising interventions can itself have unwanted consequences. Arguably the most reasonable position to take in the UK is to support relatively liberal approaches to supplying both 'weak' and 'strong' opioid based treatments when these are likely to confer clinical benefit, in an overall environment that assures universal access to comprehensive, good quality health and social care for individuals suffering persistent pain and which firmly resists pressures to provide excessive volumes or otherwise inappropriate supplies of any prescribed drug.

Another potential area for drug misuse is that of over-the-counter (OTC) medicines, perhaps most notably those containing codeine. Whilst there is little robust information on the scale of addiction to and misuse of OTC medications in the UK, there is nevertheless evidence it does exist (All-Party Parliamentary Drugs Misuse Group, 2008). Addiction to medicines like codeine can begin when someone in pain finds that their normal dose does not sufficiently reduce their pain, perhaps due to the onset of opioid tolerance. They may therefore intentionally or unintentionally begin to exceed the recommended usage amounts and/or durations.

Some medical observers may argue that such risks imply that pharmacy based supply of such treatments is inherently undesirable. An alternative view, favoured here, is that improved pharmacy access to primary care patient records (or the separate development of comprehensive pharmacy and prescribed drug

use records, as in Sweden) could significantly reduce any such risks without inconveniencing or imposing needless costs on the majority of the population living with little or no risk of abusing OTC medicines.

Finally, even drugs like paracetamol, which is available as a General Sales List medicine in many retail shops, can be abused with potentially lethal results. For instance, there is research demonstrating that people who repeatedly take doses of paracetamol that are higher than recommended in order to 'top-up' their pain relief are at risk of 'staggered overdosing'. When this occurs they have a lower chance of survival than individuals who take single intentional overdoses (Craig *et al.*, 2011).

The fact that limited volumes of paracetamol are (like many other drugs and potentially hazardous non-pharmaceutical products) easily accessible by members of the public enhances self-care opportunities and does not present a significant risk to the great majority of informed 'normal' users. Yet a very small minority will experience undesirable consequences. This has led to some calls for tighter controls. However, the available evidence suggests that maximising overall public wellbeing while protecting the more vulnerable will not be achieved simply by more stringent drug access regulations. Rather, it is more likely to be achieved by further developing policies that promote socio-economic equity together with universal access to comprehensive, good quality, health and social care.

Specialist pain services in hospitals and the community

The initial findings of the National Pain Audit (Dr Foster Research, 2011) referred to earlier reveal a mixed situation in England and Wales. On the one hand some 214 local NHS pain services were identified, which is encouraging given that as a specialism pain management is relatively new. On the other hand these appear to be of variable quality and unevenly distributed, so that while some areas enjoy more than one service others have none. (Previously reports have shown a six-fold difference in primary care organisation funding for pain management services – Chief Medical Officer, 2008).⁴

Some two thirds of English pain services identified in the new National Audit and four fifths of those in Wales described themselves as multi-disciplinary. However, these proportions dropped to just over one third and three fifths respectively when the criteria set by organisations such as the British Pain Society were applied. It is reported that many services do not have the level of technical support needed to provide good quality information about their patients and treatment outcomes, and that few have the capacity to train new staff.

⁴ See also www.rightcare.nhs.uk/index.php/atlas/atlas-of-variation-2011

Critical commentators have suggested that traditional pain clinics tend to put a great deal of emphasis on treating specific areas affected, and may have been seen as somewhere to use only as a last resort. Patients often experienced long waits before being referred, and when the latter occurred it was often without the GP involvement. This not infrequently led to avoidable co-morbidities and entrenched patterns of counter-productive behaviour (Pain Management Solutions).

Modern pain services seek to act in a timely and holistic way, with a coordinated team of health professionals conducting comprehensive assessment of pain and its impact on patients and their families. This should lead on to the co-ordinated implementation of tailored management plans which as appropriate utilise several therapeutic modalities, including pharmacological interventions, physical therapy, psychological therapy and social support designed to help service users cope more effectively with their pain. The majority use CBT along with relaxation therapy, goal setting and pacing, education about the physiology and pharmacology of pain and progressive supervised physiotherapy exercises. Some pain clinics may also offer pain management programmes (PMP) which are psychologically-based rehabilitative treatments where pain relief is not the primary goal (Hobbs & Knaggs, 2011).

Patient improvement is ideally measured by monitoring factors such as mood, the occurrence of catastrophising thoughts (which is inversely linked to psychological resilience), physical performance, overall function and the appropriate use of drug treatments, rather than simply the reduction of reported pain (Chief Medical Officer, 2008). It is claimed that patients managed via such multidisciplinary programmes have lower overall healthcare costs, return to work more frequently and experience greater pain control as compared with those managed with more traditional biomedical models. There is good reason to believe this to be so, although the need to collect outcome data more systematically than is presently the case should not be forgotten in this context.

As the preliminary findings of the National Pain Audit indicate, the design and level of integration of specialist pain management services can vary greatly (International Association for the Study of Pain, 2004). The available data shows that only about 30 per cent of pain clinics in the UK collect outcome data systematically: this may have undermined attempts to improve funding, not least because the term 'multidisciplinary' seems sometimes to be regarded as synonymous with 'expensive' (Phillips et al., 2008; Pain Proposal Committee, 2011). Reported access times to pain clinics range from a few months, most often in the case of GP referral, to over a year. The international literature indicates that it is still frequently the case that people access pain centres only after lengthy experiences with pain, averaging in the order of seven years (International Association for the Study of Pain, 2004).

In addition to improving the early identification of chronic pain, one way of remedying such service limitations is to enhance the availability of specialist pain management in the community setting. In Nottingham, for example, a community-based multidisciplinary team, led by a consultant in pain medicine, has the support of specialist physiotherapists and clinical nurse specialists in pain management and spinal surgery. They work together with consultant spinal surgeons, physiotherapists, occupational and cognitive behavioural therapists and an advanced pharmacy practitioner across community and secondary care environments (Hobbs & Knaggs, 2011).

This has resulted in accelerated patient access to MRI, rehabilitation programmes, minor interventional procedures and more complex surgical intervention if required. Both GPs and patients are reportedly highly supportive of this community pain service, which has also helped to enhance working relationships between primary and secondary care clinicians. The 'meso-level integration' that can consequently be achieved (Curry & Ham, 2010) helps support individuals with care needs that straddle traditional professional and organisational boundaries. Service commissioners should be informed of the health outcome benefits and efficiency generating potential of such innovations.

Improving primary care

Primary care, the provision of which throughout the UK encompasses the nurses, doctors, pharmacists and other health professionals working in GP surgeries, dental practices, community pharmacies and high street optometrists, is where the majority of individuals with persistent pain present. It has been estimated that across Europe only two percent of people who experience persistent pain are seen by a pain specialist (Breivik et al., 2006). Given the massive scale of both acute and chronic pain related problems and the complex links between them, such figures highlight the need for triage and efficient and effective pain management in primary care. Yet as noted earlier in this UCL School of Pharmacy report, the present level of education, confidence and ability of many doctors and other health professionals in this important field appear limited, along with reported service user satisfaction. Although over time enhanced educational standards should help to correct such imbalances, there is arguably a need for more urgent changes than those which can be delivered via interventions such as revised academic curricula.

One immediate problem is the apparent lack of use of validated pain assessment instruments in primary care. An extended application of such measures in a variety of community settings will very probably be required if rates of chronic pain risk factor detection and early stage treatment are significantly to be improved. Yet it has been estimated that currently only 15 per cent of persistent pain sufferers have been assessed with a pain scale. Greater use of the relatively simple instruments involved could allow personal health

service providers such as GPs, nurse practitioners and community pharmacists to identify people with 'red-flags' such as weight loss, psychological problems and possible signs of, say, cancer or other underlying causes of pain.

As appropriate, this would permit such patients to be referred on to specialist services for further investigation and treatment in as timely a manner as possible (Hobbs & Knaggs, 2011), albeit that the aim of cost effective primary care provision is to minimise the unnecessary use of costly secondary care resources. Awareness of the importance of the latter highlights the desirability of delivering effective pain care within the primary care setting whenever possible, in part through the guideline/protocol/pathway informed use of medicines and psychological treatments such as CBT.

However, it should be recognised that in practice using guidelines such as those from the BPS may be more difficult than their authors may hope. Similarly, NICE guidelines like those for neuropathic and low back pain are only effective if healthcare professionals have the time and resources to work with them, and are able to determine what kinds of pain their patients are experiencing. Hence some authorities have argued that chronic pain management should become a NICE Quality Standard, and that performance in persistent pain prevention and treatment should be included in the Quality and Outcomes Framework (QOF) and/or other primary care contractual arrangements (Beavers, 2011).

There are valid concerns that poorly designed 'pay for performance' based incentive systems risk narrowing the attention of health professionals, so that they tend to focus mainly on rewarded activities. This can undermine the holistic approaches needed for the effective management of complex biopsychosocial disorders like persistent pain. But at the same time facilitating transformed patterns of care inevitably requires investment, and realistic approaches to encouraging health care providers to accept changed ways or practice that should ultimately lead to efficiency savings.

Following on from the above, more informed and effective involvement of community based pharmacists in pain management, who are often not only the first health care workers a patient in pain will consult but also the professionals to whom many people on long term therapy are most likely to confide in, could arguably improve the management of persistent, mixed and acute pain at both the individual and population levels. Issues relating to this opportunity are discussed below.

New approaches to pharmaceutical care

From a pharmaceutical care perspective there are two fundamentally important pain related tasks to be achieved in the coming 10-20 years. The first is to continue developing new pharmaceutical treatments

that will control acute and chronic pain better and with fewer unwanted side effects than is currently possible, or prevent or treat pain related conditions such as rheumatoid and osteoarthritis or multiple sclerosis more effectively than is currently possible. This is primarily the responsibility of the pharmaceutical industry, working in collaboration with academic partners. But professionals such as pharmacists can affect factors such as the uptake of new (and inevitably relatively costly) treatments in conservative settings such as the NHS.

The second is ensuring that across the globe, in rich and poor communities alike, established medicinal and other complementary evidence based interventions for the effective treatment of pain such as psychological interventions, are as universally and cost effectively available as possible. This is an end to which modern pharmacy could make critically important contributions.

No single drug can successfully treat both the nociceptive and neuropathic components of pain. As in many other areas of pharmaceutical innovation, research in this area has proved more time consuming and technically challenging than was in the past hoped. However, despite the fact that stakeholders believe that pain research is underfunded, progress is being made. Continued investment will ultimately mean that humanity will gain significantly improved means of preventing and treating painful conditions, but also pain itself. Once innovative therapies have outlived their intellectual property protection, they typically become available for mass access at a very low marginal cost. By contrast health gains associated with inputs such as, say, good nursing or surgical skills are always likely to cost a similar amount. This fundamental difference makes it in the long term very much more cost effective to invest in a new medicine than most other forms of health care that at the time of their introduction provide comparable benefits at comparable costs.

Such arguments add weight to the view that when new pharmacological treatments are developed they should be made available to patients as promptly as possible. Delaying uptake saves money in the short term. But it harms the interests of health service users and undermines the funding mechanisms vital for supporting long term pharmaceutical technology driven efficiency gains. This is contrary to UK and wider public interests.

One interesting example of a recent analgesic medicine development is called tapentadol (Dickenson, 2011). This drug has dual effects on opioid receptors in ascending pathways and noradrenaline receptors in descending pathways in the spine. Clinical trial data suggests its use is associated with a lower incidence of opioid side effects than other drugs commonly in use. In May 2011 it was accepted for use by the Scottish Medicines Consortium for use in patients with severe persistent pain who could be adequately managed only with opioids.

With regard to research in progress nerve growth factor (NGF) is a neurotrophin (nervous system protein) that

regulates the structure and function of responsive sensory neurones, including small diameter nociceptor neurones. Antagonising (opposing) the effects of NGF results in pain relief in many acute and persistent pain states (Hefti et al., 2006). Tanezumab, a monoclonal antibody for NGF which blocks the interaction of NGF with its receptors is currently undergoing clinical trials to determine its effectiveness in a number of persistent pain states. In Phase II trials it was shown to produce sustained effective pain relief in osteoarthritis (Lane et al., 2010) and low back pain (Katz et al., 2011). However, in later trials involving 6800 patients, 16 went on to develop worsening osteoarthritis and required total joint replacement of their knee, hip or shoulder. This led to the halting of all clinical trials involving the drug along with trials for other NGF monoclonal antibodies (Ray, 2011).

This example illustrates the risks of investing in pharmaceutical research, and the types of challenge that have to be overcome in bringing a new medicine to today's highly regulated international marketplace. It has been suggested that the joint worsening might be due to excessive 'wear and tear' in the absence of protective joint pain (Wood, 2010), or a reduction in NGF-dependent nerve fibres which also control blood flow through tissues (Ray, 2011). If the latter hypothesis is correct this could in future lead to a new understanding of some forms of painful musculoskeletal disease. Research on tanezumab and related opportunities continues. Even if it is not immediately successful, there remains a robust possibility that targeted small molecule drugs based on NGF antagonism will eventually be developed (Hefti et al., 2006). This could in time bring significant benefit to all communities.

'Voltage gated sodium channels' (Na_v s) are another key target for pharmaceutical industry and University based pain researchers. These play an important role in controlling action potential propagation and potentiation. Altering their function or expression can hence have a profound effect on normal cell excitability. There are multiple Na_v isoforms (that is, slightly differing forms) which have varying distributions and electrophysiological and pharmacological properties. Four in particular are potential targets for novel analgesics (Theille & Cummins, 2011):

- $\text{Na}_v1.3$ – The predominant isoform in the CNS and PNS during embryogenesis, although expression in the PNS reduce in adulthood. Following nerve injury and inflammation amounts of the channel increase in the periphery, indicating that they play a role in pain perception. Patients with trigeminal neuralgia also have increased expression of the $\text{Na}_v1.3$ channels.
- $\text{Na}_v1.7$ – This isoform is expressed in sensory and sympathetic PNS neurones. People suffering from congenital insensitivity to pain have truncated, non-functional, $\text{Na}_v1.7$ channels (see Box 5, page 15).
- $\text{Na}_v1.8$ – These channels play a role in both visceral (nociceptive) and inflammatory pain, and may be

involved in certain types of neuropathic pain. They are only expressed in peripheral sensory neurones and carry the majority of action potentials in nociceptive neurones.

- $\text{Na}_v1.9$ – This is another peripheral isoform. It plays a predominant role in inflammatory pain, but not in neuropathic pain. It could be involved in determining pain thresholds, and is currently considered to be an attractive target for new medicines designed to modulate pain sensitivity.

Selective blockers of the $\text{Na}_v1.7$ and $\text{Na}_v1.8$ channels have been shown to be effective in rat models of neuropathic pain (Theille & Cummins, 2011). Additional research in humans is warranted to determine if selective blockade of the pain-related Na_v channels would result in an analgesic effect.

Finally, gene therapies may also be developed for persistent neuropathic pain. If they prove successful, they will work by introducing specific genes into neurones where they interact with the receptors and ion channels involved in pain mediation. Examples include those that encode proteins with antinociceptive properties, and those that are antagonists of nociceptive molecules.

Delivering such genes to the desired sites of action requires a vehicle in the form of a viral or non-viral vector. In animal models, several trials of technologies targeting opioid, cytokine, GABAergic and noradrenaline (norepinephrine) pathways have resulted in effective analgesia (Kumar et al., 2011). A human Phase I trial involving gene therapy for analgesia has also recently been completed. The researchers involved used a replication-defective (in essence, inactivated) herpes simplex virus to deliver the PENK gene (human pro-enkephalin) to neurones in the spine. The intervention was found to be safe and well tolerated and gave a dose-responsive analgesic effect. Such observations indicate that further clinical investigation is warranted (Fink et al., 2011).

Innovative approaches to delivering community pharmacy services for people with pain

This report estimates that at any one time there are in the order of one million people in the UK with a persistent pain condition that could have been prevented or be being relieved more effectively. However, the magnitude of the problem of pain is far greater. The available evidence suggests that around twenty per cent of the overall population is living with significant pain, approaching half of whom are likely to be in relatively severe distress. Such data underline the fact that although developing specialist services is an important priority, at a population level further improving the pain management performance of mass access 'normal contact' primary care services such as a community pharmacy should play a critically important role in providing a sustainable, affordable way forward.

As Table 3 outlines, pharmacists already offer – in addition to their core dispensing role – competencies and services relevant to the needs of people living with and receiving treatments for pain. As previously described, there is evidence that in the order of 80 per cent of the public already say that acute pain is a symptom/condition they would consult their pharmacist about (Carr 2011). This is a strong base to build on in relation to re-engineering pain care related pathways, and extending community pharmacists' contributions to enhancing health outcomes via not only signposting to other services, but being more directly involved in case finding, diagnostic activity and, as appropriate, treatment initiation and monitoring.⁵

It would be beyond the scope of this report to offer a detailed description of how and why community pharmacy is evolving in the direction of providing a wide range of public health oriented and clinical care linked services in addition to its more traditional medicines supply role. But key points include:

- Community pharmacists were originally intimately involved both in making medicines and providing health care directly to the public. But as the modern pharmaceutical industry and the NHS developed, the focus of their role shifted towards dispensing and monitoring prescribing quality. Now computer based technologies are mechanising aspects of this work, while better working age population health and the ageing of the community is creating demands for new forms of easily accessible primary health care.
- In England this has led to the funding of new 'cognitive' services involving prescribing and allied activities, such as repeat dispensing management, conducting Medicines Use Reviews (MURs) and supporting patients who are in receipt of new medicines (the NMS). In Scotland there has been a greater emphasis on areas such as chronic disease management, although the underlying direction of change is similar.
- Pharmacists have also sought to develop roles in 'public health' fields such as smoking cessation and weight management, and areas such as cardio-vascular risk testing. Initiatives such as the establishment of 'Healthy Living Pharmacies' in areas like Portsmouth are intended to build further on such progress, linking health promotion work to the building of well managed pharmacy teams committed to health improvement, and the extension of pharmacy services in areas such as case finding and the direct delivery of pharmaceutical care.

There are widely recognised, and significant, barriers to community pharmacists becoming better established as a cost effective first tier access point in the NHS and other health care systems. But to the extent that this proves achievable, preventing and treating acute and chronic pain is the type of health problem that

they should be well placed to address successfully in the future (McDermott et al., 2006). Although the available evidence suggests that to date new pharmacy services such as MUR provision are unlikely to have made significant contributions to cancer or chronic pain management (Blenkinsopp et al., 2011), better targeted interventions should nevertheless have the capability to do so. Conducting well focused MURs could, for instance, furnish pharmacists with opportunities to help people use prescribed opioid and other analgesics effectively and safely (Youssef, 2010). Other interventions that a systematic, and where necessary information technology facilitated, approach to community pharmacy based pain management could provide include:

- self care support, including where needed improved public protection against potentially harmful over-use of 'minor' analgesics such as paracetamol and NSAIDs and informing public understanding of what types of pain should be either accepted and 'worked through', or referred to GPs and/or specialists;
- opening the way to an extended use of assessment instruments to identify persistent pain risks, and cases; and
- signposting psychological and other care providers, or facilitating patient use of relevant computer based services.

Community and other pharmacists could and probably should in addition work in collaboration with local GP surgeries to provide better pain management. Specialised independent pharmacist prescribers, who can issue prescriptions, could for instance run weekly or monthly pain clinics and in some instances assume a direct case management role. This could reduce GP workloads and extend patient choice in ways that should also reduce pressures in hospital based services, especially if good working links with the other community based teams are developed. One such clinic is undergoing a six-month pilot trial in Whitton in Essex, involving 30 persistent pain patients. Although this project faces a number of challenges (Rose, 2011) it may well provide a pointer to the ways in which pharmacy could and should in future provide enhanced services to the communities it serves.

Conclusion

The relief of pain has been important in all human societies throughout history. But in 'post transitional' countries like today's Britain it is even more of a challenge than in the past. Although the treatment of acute pain in contexts such as accidental injury is now more effective than ever before, persistent pain associated with the epidemiological changes characteristic of population ageing and the lifestyles linked to late stage 'post industrial' development has become increasingly prevalent. If in future welfare service costs are to be maintained at affordable levels, and older people helped to live independently and

⁵ Clinical pharmacists working in the hospital setting can also play central roles in pain monitoring and medication management (Kumar, 2007).

Table 3. Some illustrative examples of Pharmaceutical Care

Pharmacy user's concern	Potential reason	Pharmacist intervention
Customer/patient presents with pain with a 'red flag' indication such as a headache in a child, accompanied by skin rash or stiff neck; an adult with a very sudden and/or severe onset headache; significant pain of unexplained origin in individual with a history of cancer.	Pain may be indicative of a dangerous condition such as meningitis or a cancer recurrence.	Pharmacist should refer the pharmacy user to the most suitable location, such as their GP or an A&E department, in a manner designed to minimise needless anxiety but support appropriate action
Codeine not working for pain relief	The individual may be one of the 10 per cent of the population lacking the enzyme for drug activation	Advise patient to request an alternative opioid from their GP, or offer an alternative Pharmacy or GSL medicine
Pharmacy customer presents with pain of relatively recent origin, and a 'yellow flag' indication such as being socially withdrawn, depressed and/or anxious, or reporting cessation of normal physical activity	Subject may be at risk of develop a persistent pain problem	Pharmacist discusses the causes of chronic pain states, and ways in which they may be avoided. A pain assessment could be offered. Patients with a number of yellow flags may warrant early referral to a pain management specialist.
NSAIDs not working for pain relief	Patient may have neuropathic or multiple pain, the neuropathic element of which will not be alleviated by an NSAID	A pain assessment could be conducted. Alternative or additional drug choices should be discussed, and/or the individual advised to consult their GP or alternative prescriber.
Patient says they do not know who to turn to about their persistent pain	Evidence of an inadequately resolved health problem, a lack of clear and concise information available	Patient distress should be evaluated, and if necessary emergency action initiated. Service user should be encouraged to expect adequate relief information leaflets and links to relevant patient support websites should be available in pharmacies to augment the face-to-face consultations
Patient is concerned about being prescribed an antidepressant for pain	The individual may not be aware that antidepressants are used off-licence for pain relief, and that the prescription does not imply mental illness	Pharmacist explains the adjuvant use of anti-depressants and other drug classes for analgesia, and provide support and information as required
Patient reports unacceptable side effects, such as (for instance) undue drowsiness, problems like vomiting and/or restlessness and agitation, or constipation	Other health professionals may not have discussed (or the health service user may have forgotten warnings about) possible side effects and/or drug-drug interactions. For example, taking medicines such as Tramadol and an SSRI simultaneously may result in serotonin syndrome; taking alcohol with opioids can cause drowsiness	A 'MUR plus' review should allow full discussion of treatment options and medicines taking/use related problems and concerns. The benefits of taking analgesic medicines regularly as advised as opposed to PRN use should be explained to people living with persistent pain. Patients prescribed opioids can benefit from being supplied with laxatives on a preventive/for early use basis
Customer has purchased OTC codeine on multiple occasions, or there is reason to believe he or she is obtaining codeine from a variety of sources	Patient may have developed an addiction	Discuss the situation to explore the nature of the experienced problem. For instance, pseudo-addictions may develop because of ineffective pain treatment. Medication reviews and/or a pain assessment may be required. Signposting towards effective support and/or advice about obtaining more effective treatment could be given.
Customer has purchased other OTC analgesics such as paracetamol containing products on a variety of relatively recent occasions	The individual may have an inappropriately managed persistent pain problem, or be over-using minor analgesics in a potentially counter-productive and or hazardous manner	The pharmacist could offer to conduct a brief pain assessment and as appropriate provide advice. If the service user needs more assistance and/or direction the pharmacist could refer them to their GP or if the option is available directly to a community based pain clinic.

Pharmacy user's concern	Potential reason	Pharmacist intervention
Patient reports having a backache of recent onset	This may be an acute back pain which can last for 3 months, but which can normally be self managed and will eventually resolve	A past history of significant illness such as breast or prostate cancer would justify referral to the patient's GP. Otherwise the pharmacist may advise that daily activities should as far as possible be continued, and that effective doses of analgesia should be taken. Help with lifestyle changes such as weight loss and good posture/lifting techniques could also be offered
Customer requests information about using Fentanyl patches	Patient has not received information from other sources, or may have other undisclosed concerns	Pharmacist could advise that Fentanyl patches can be useful for persistent pain and are safe provided due care must be taken. For example, the risk of taking a hot bath while wearing a patch should be explained to the patient. People with persistent pain may fear that it is caused by cancer even when this is not the case. Pharmacist interventions can help reveal undisclosed fears, and support their resolution
Patient with a history of pain is concerned about being prescribed 'tranquillisers', or reports an abnormal mental state on completing treatment for a musculo-skeletal condition	The individual may not have been adequately informed of the muscle relaxant properties of benzodiazepines, or has abruptly stopped taking a benzodiazepine	Explain the relevant drug actions. If a potentially hazardous withdrawal reaction is suspected refer to the prescriber, and as necessary initiate protective intervention

productively for as long as possible, addressing pain more effectively needs to be accepted as a central national health improvement goal.

In the medium to long term new medicines and other treatments will help reduce the extent of the pain, disability and handicap caused by musculoskeletal, neurological, metabolic and other common disorders, including osteoarthritis, multiple sclerosis and diabetes. It should also provide more effective ways of treating persistent pain conditions which exist as functional diseases in their own right, like fibromyalgia. But although such science based progress will certainly be achieved over time (provided that relevant academic and industrial research continues to be funded) the technical, regulatory and allied challenges involved are such that its delivery cannot be assured within the next one to two decades. More immediate forms of intervention are therefore needed to help the million or more individuals who are in this country alone at any one time living with pain that could and should be better managed.

Success in this respect will demand complementary actions at all levels, from the provision of specialist bio-medical and psychological support in secondary and tertiary settings through to improvements in the working of the primary care system as a whole, and the implementation of public health programmes designed to inform and support communities and individual's self management strategies. One vital message to communicate is that although once a chronic pain state has been established, or is at the point of starting, it is important to access good professional advice, it is equally important not to needlessly medicalise episodes of acute pain and to wherever possible 'keep going' despite experiencing pain. Many people at raised risk of suffering extended periods of chronic pain appear to over-estimate the benefits of resting and suspending their everyday activities, perhaps in part because of exaggerated fears that they will further damage themselves if they continue living normally.

There is a powerful case for investing more in specialist pain management services, especially in under-served areas. However, in the current financial situation the capacity of the NHS to devote additional resources to any end is limited. In addition, the analysis offered here makes it clear that the numbers of people living with and/or at high risk of chronic pain are so great that specialist service provision alone cannot significantly impact the overall population level pain problem. In such circumstances diffusing relevant knowledge and competencies through the health care and wider communities, and making best use of existing resources, is also vital.

Developing community pharmacy in contexts such as pain management represents one such opportunity. To the extent that technical developments will in future contain or further reduce dispensing costs, pharmacies represent an asset that could deliver extended contributions to both public health and the clinical care of individuals. However, this depends on not only the willingness of pharmacists themselves to change their ways of practising, but the willingness of other professional, managerial and other stakeholders-including most importantly GPs and people with long term illnesses themselves – to accept the need for new health care models.

In an area as important and potentially sensitive as health care any form of innovation must be introduced with care, and is likely to encounter opposition. But the case for further change in the prevention and treatment of persistent pain is particularly strong, because of the weight of evidence from across the world that traditional bio-medical approaches have failed to serve patients as well as should be possible. If the optimal relief of avoidable suffering is taken as the highest priority goal of health care, then all professionals should be open to the development of better ways of managing pain.

Pain resource site links

The new UCL School of Pharmacy UK CPA pain discussion guide for community pharmacists 'Talking About Pain' can be found via the School of Pharmacy website www.Pharmacy.ac.uk

There are multiple pain-self help guides published online that may be useful for both patients and pharmacists. The most comprehensive of these, 'PainXchange' was designed in Australia. It contains useful information on assessment and management tools (<http://www.painxchange.com.au/Default.aspx>).

An alternative tool kit 'Treatment Options' (<http://www.painknowledge.org/opioidtoolkit/docs/Treatment%20Options.pdf>) is another useful source. It aims to help educate patients and their carers about treatment options, including non-drug possibilities, and offers questions to ask healthcare workers. It was produced by the American Pain Foundation, and although oriented to US requirements is a substantive resource.

A similar publication has been produced by the British Pain Society called 'Understanding and managing pain: information for patients'. It also serves as an educational resource for patients on what pain is, what can be done about it, who can help and how people can help themselves (http://www.britishpainsociety.org/book_understanding_pain.pdf).

Change Pain is an educational programme funded by a pharmaceutical company that has products used for the management of pain. It offers a useful pain assessment tool (<http://www.change-pain.co.uk/>).

Finally, an additional resource is the Chronic Pain page of the Health Talk Online website (http://www.healthtalkonline.org/chronichealthissues/Chronic_Pain). This contains large amounts of information on management and treatment as well as data from interviews with persistent pain sufferers.

Multiple different types of pain scale have been discussed in the paper. They include for the assessment of neuropathic pain the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), the DN4 for neuropathic pain, and PainDETECT :

DN4 = http://www.painxchange.com.au/AssessmentTools/Appendices/PDF/Apx3_DN4.pdf

LANSS = http://www.painxchange.com.au/AssessmentTools/Appendices/PDF/Apx4_LANSS.pdf

PainDETECT = http://www.virtualmedicalcentre.com/calc_pfizer_pain_detect.asp

A variety of assessment tools for use in neonates, infants and children exist. Using FLACC, neonates and patients unable to communicate verbally are scored on a number of behavioural cues in five measurement areas – faces, legs, activity, cry and consolability (<http://bcmartin.yolasite.com/resources/FLACCSCALE.pdf>).

Similarly, the neonatal facial coding system (NFCS) uses facial behaviours such as brow lowering, vertical mouth stretch, taut tongue and lip pursing to monitor pain: (https://www.cebp.nl/vault_public/filesystem/?ID=1425).

The Premature Infant Pain Profile (PIPP) uses gestational age, behavioural cues, and various physiological measures such as heart rate and oxygen saturation to get a measure of the pain caused by various procedures (https://www.cebp.nl/vault_public/filesystem/?ID=1467).

The COMFORT scale provides a pain measurement in unconscious and ventilated infants, children and adolescents (<http://www.cincinnatichildrens.org/assets/0/78/176/4711/4717/e0808b3f-49b9-4196-b696-85148aa158cb.pdf>).

CRIES is based on five categories (cries, requires oxygen, increased vital signs, expression and sleepless) each of which is scored between zero and two to give an overall score: (http://painconsortium.nih.gov/pain_scales/CRIESpainScale.pdf).

Two self-report based measures of pain in childhood are also available. Firstly, the Pieces of Hurt instrument involves four poker chips, described as pieces of hurt, being placed in front of the child. The first chip is 'just a little hurt', the second is 'a little more hurt', the third is 'more hurt' and the fourth chip is 'the most hurt you could have'. The child is asked 'How many pieces of hurt do you have?'

The Faces Pain Scale Revised involves the child choosing a face to represent the pain they are feeling (<http://www.iasp-pain.org/Content/NavigationMenu/GeneralResourceLinks/FacesPainScaleRevised/default.htm>) and can be used in slightly older children than the Pieces of Hurt method.

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