An overview of treatment approaches for chronic pain management

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Abstract

Pain which persists after healing is expected to have taken place, or which exists in the absence of tissue damage, is termed chronic pain. By definition chronic pain cannot be treated and cured in the conventional biomedical sense; rather the patient who is suffering from the pain must be given the tools with which their long-term pain can be managed to an acceptable level. This article will provide an overview of treatment approaches available for the management of persistent non-malignant pain. As well as attempting to provide relief from the physical aspects of pain through the judicious use of analgesics, interventions, stimulations, and irritations, it is important to pay equal attention to the psychosocial complaints which almost always accompany long term pain. The pain clinic offers a biopsychosocial approach to treatment with the multidisciplinary pain management programme; encouraging patients to take control of their pain problem and lead a fulfilling life in spite of the pain.

Keywords: chronic pain, pain management, biopsychosocial, psychology

Introduction

Pain is a common symptom of numerous medical problems, which usually indicates the occurrence of tissue damage. Whilst pain is unpleasant, it is also a useful mechanism with which to promote healing – forcing the sufferer to rest the affected area and seek out medical assistance. Pain associated with tissue damage, inflammation, or a disease process that is of relatively brief duration (days or weeks), is usually referred to as acute pain. When pain persists for extended periods of time – either as an accompaniment to a disease process, or following the usual amount of time expected for an injury to heal – it is referred to as 'chronic pain' [1]. The International Association for the Study of Pain (IASP) have defined chronic pain as that which lasts for longer than three months [2]. The pain persists long after it can serve any useful function and is no longer just a symptom of injury or disease but a medical problem in its own right [3]. 'Chronic pain' describes a syndrome characterised by persistent physical pain, disability, emotional disturbance, and social withdrawal symptoms existing together and influencing one another in what Bandura [4] termed 'reciprocal determinism'. The source of the physical pain may be known or unknown: regardless, the sufferer of chronic pain will undergo a number of biological, psychological, and social upheavals over the course of their illness. In order to explain such a complex syndrome as chronic pain, we must not become fixated on finding biomedical causes, but also consider the roles of the psychological and social dimensions [5]. In what Jacobson and Mariano [6] have called a 'biopsychosocial systems model', people are viewed as living systems with multiple levels of analysis ranging from the cellular to the social. From this perspective, all three (bio, psycho, and social) dimensions of the model are given equal importance in their influence on personal experience.

Following this biopsychosocial approach, we may expect to find that treatments for chronic pain are a mix of medical, physical, and psychological components. Such treatments do exist in the context of a pain clinic, where several disciplines of pain treatment are delivered simultaneously. However, patients are seldom referred to multidisciplinary treatment as soon as their pain becomes chronic [7]. More often, the patient is treated as though they are suffering from an extended period of acute pain, which means that numerous medications and interventions are tried and tested, with the goal of reducing the pain to an acceptable level. This review will describe the range of treatments which exist for the management of pain, in the approximate order by which they are applied to the sufferer of chronic pain.

Methods

A narrative review of studies investigating treatment approaches for the management of chronic pain was carried out according to published guidance on narrative reviews [8]. We searched MEDLINE and EMBASE up to November 2nd, 2015. A combination of MESH and free text terms was employed including pain, chronic pain, analgesics, opioids, neuromodulation. Studies were selected for inclusion if examining treatments for the management of chronic pain. The search was restricted to articles published in English. A hand-search of the reference lists of studies meeting the inclusion criteria was also performed.

Analgesic Medication for Pain

Conventional oral analgesics are always the first treatment given; they can be a fast, cheap, and relatively safe solution to the problem of pain. There are also a large number to choose from. In treating a case of pain the physician usually follows the steps on the World Health Organisation (WHO) analgesic ladder (Figure 1) [9]. Initially developed for the treatment of cancer pain, but applicable to most pain conditions, the ladder suggests that analgesic medications should be given orally with increasing dose and potency until pain relief has been achieved. It is a simple and inexpensive approach that produces pain relief in 80-90% of cancer patients [10]. When applied to chronic non-cancer pain, patients rarely achieve long-term pain relief as side-effects tend to limit maximum dosage, and mean pain relief from opioids has been reported to be around 30% [11].

Non-Steroidal Anti-Inflammatory Drugs

The first step of the ladder consists of non-opioid analgesics, such as paracetamol and the non-steroidal anti-inflammatory drugs (NSAIDs). These act to reduce inflammation and provide pain relief, reducing the production of inflammatory chemicals by inhibition of the cyclooxgenase enzymes COX-1 and COX-2. These enzymes catalyse the production of two types of eicosanoids: prostaglandins (PGs), which cause vasodilatation, increase vascular permeability, sensitise nociceptors, and inhibit gastric acid secretion and platelet aggregation; and also thromboxanes (TXs) which cause platelet aggregation and vasoconstriction. COX-1 is constituent to most tissues of the body, producing PGs and TXs for tasks such as gastrointestinal (GI) protection, maintenance of renal blood flow, and platelet aggregation [12]. By contrast COX-2 is mainly induced in inflammatory cells in response to damage, and is therefore chiefly responsible for the effects of inflammation – including pain [13]. Non-selective COX inhibitors act on both COX-1 and COX-2 and include aspirin, ibuprofen, and naproxen. The side-effects of these drugs are mainly due to their inhibition of COX-1. GI ulcers and their complications occur in 2% to 4% of patients on high doses [14] and for this reason they are often administered alongside a proton-pump inhibitor to protect the stomach lining from acid secretion. Selective inhibitors of the COX-2 enzyme (coxibs), including celecoxib and etoricoxib, were developed in the early 1990s and subsequent studies showed that pain relief could be achieved without the gastrointestinal and renal side effects of the traditional NSAIDs [14–16]. However, once the coxibs were in widespread use a number of controlled trials revealed a strong association with increased risk of serious thrombotic cardiovascular (CV) events [17–21] and many were withdrawn. Coxibs have since been shown to suppress COX-2 mediated production of platelet PG-I2 (an inhibitor of platelet aggregation) but not COX-1 mediated TX-A2 (a promoter of platelet aggregation), thus promoting a prothrombotic vascular state [22–24]. By contrast, the non-selective NSAIDs somewhat suppress platelet TX-A2 production through COX-1 inhibition; however they do vary in degree and duration of platelet COX-1 inhibition [25, 26] and have also been linked with an increased risk of thrombotic events [27]. More recent meta-analyses of long-term use of high dose NSAIDs have found that all increase the risk of coronary heart disease (CHD) and thrombotic CV events to some extent [28–30] (with the exception of naproxen, which has a long lasting suppressive effect on TX-A2 production [25, 26]). The European Medicines Agency's Committee for Medicinal Products for Human use (CHMP) guidelines contraindicate the use of coxibs in patients with CHD or stroke, and recommend caution when used for patients with risk factors for CHD [31]. The CHMP also concluded that the benefit-risk balance for non-selective NSAIDs is favourable, but emphasise judicious use based on individual patient risk factors [32]. If high doses of NSAIDs are required to control pain, it is sensible to make use of alternative treatments in the first instance rather than expose those patients to the cardiac, GI, and renal risk of long-term use.

Weak and Strong Opioids

The second step of the ladder adds weak opioids, codeine and dihydrocodeine. Opioid drugs mimic the effects of naturally occurring pain reducing chemicals (endorphins) which activate opioid receptors in the central nervous system that attenuate transmission of nociceptive signals. Long-term use (>180 days) of codeine carries an increased risk of CV events in older patients [33]. The third step calls for strong opioids, which are more potent but also have more severe side effects than weak opioids. Opioids suppress nerve activity via activation of G-protein coupled opioid receptors which promote K^+ (causing hyperpolarisation) and inhibit Ca^{2+} (reducing transmitter release) entry into the nerve cell [12]. Endogenous opioid networks are involved in the regulation of many physiological functions as well as pain; therefore side effects always accompany administration of opioid medication. Respiratory depression occurs at therapeutic doses and can be fatal, so patients are always started at a low dosage which can be increased as tolerance develops. Also nausea, constipation, cognitive impairment, sedation and various hormonal effects are concerns with chronic opioid use [11]. The nervous system rapidly develops tolerance to the effects of opioids [34], including the analgesic effect, which means that dosage needs to be increased over time to achieve pain relief. Unlike the weak opioids, the effects of the morphine-like drugs increase as a function of dosage, therefore dose can be increased (almost indefinitely) to combat tolerance and rising levels of pain. In practice, patients tend to reach their own maximum dosage at which they can no longer accept any further increase in side effects. Recent reviews have suggested opioids for chronic pain have good short-term efficacy in musculoskeletal and neuropathic pain conditions [11], but there is less evidence for long-term efficacy beyond six months [35], which may be due to the effects of opioid tolerance and opioid induced pain sensitivity [36]. A cautious approach to dose escalation and the discontinuation of opioids if treatment goals are not met has been recommended [35, 36]. Despite widespread use of opioids in the treatment of fibromyalgia [37], there is no good quality evidence of their efficacy [38]. Opioid receptor function has been shown to be compromised in patients suffering with fibromyalgia [39], which may explain the poor response to exogenous opioids in this population. Recent work has suggested that chronic opioid use may actually worsen fibromyalgia symptoms [40], and Canadian [41] and German [42] guidelines strongly discourage their use in this condition.

Topical analgesics

The lipophilic opioids, fentanyl and buprenorphine, are suited for transdermal route of administration as they are readily absorbed through the skin, entering the blood rapidly. The use of fentanyl patches is associated with fewer side-effects than sustained-release oral morphine, including constipation and sedation, whilst providing adequate pain relief in non-cancer pain patients [43]. Buprenorphine also carries fewer side effects compared to oral morphine, and has been shown to be effective in a variety of pain conditions including osteoarthritis, low back pain, and neuropathic pain [44]. Lidocaine (an amide anaesthetic that inhibits nerve depolarisation through sodium channel blockade) can also be applied as a cream or patch to provide localised pain relief, and has been recommended for use in relief of peripheral neuropathic pain [45]. It is poorly absorbed across the skin so side effects are rare [46] and despite individual studies reporting efficacy in the relief of neuropathic pain a recent Cochrane review found no good quality evidence to support its use [47].

[Figure 1 about here]

Adjuvants

The adjuvant medications referred to by the 1986 WHO analgesic ladder are *'additional drugs... to calm fear and anxiety'* [9] that can be added at any step of the ladder. It should be noted that these are not the same as 'adjuvant analgesics', which are drugs with indications other than pain that may be analgesic in certain conditions. The terms 'adjuvant' and 'adjuvant analgesic' are conflated in pain literature; perhaps because anxiolytic drugs such as antidepressants and antiepileptics have since been found to be effective pain relievers in specific circumstances; or perhaps due to careless use of the terms which are admittedly very similar and easily confused. The adjuvants in the sense of the WHO ladder include anxiolytics to reduce pain related anxiety; hypnotics to tackle pain related insomnia; and muscle relaxants to relieve painful muscle spasm. These drugs may be added at any time depending on the individual needs of the patient.

Adjuvant Analgesics

Sometimes known as unconventional analgesics; drugs that were initially developed as antidepressants and as antiepileptics (anticonvulsants) have been found to exhibit analgesic properties when administered to patients with pain. The '+/- adjuvant' label on the WHO ladder has come to refer to these types of drugs, although it is not clear if that is what it originally meant.

In chronic pain conditions where opioid medication is often ineffective such as neuropathic pain [12] and fibromyalgia [38], some types of antidepressant drugs have been found to exhibit analgesic properties which are unrelated to their antidepressant effects. Most effective are the tricyclic antidepressants (TCAs) and serotonin and noradrenaline reuptake inhibitors (SNRIs), which both act to prevent reuptake of noradrenaline and serotonin in the brain and spinal cord. They are thought to provide analgesia by enhancing endogenous pain control and increasing the activity of the descending inhibitory pathway, however this remains unclear [48]. Selective serotonin reuptake inhibitors (SSRIs) provide little pain relief [45, 49, 50]. Antidepressants are often prescribed to chronic pain patients to treat comorbid depression and sleep problems, as well as for pain relief. After anti-inflammatory drugs and opioids, antidepressants are the most widely used drugs for the treatment of pain [51].

Antiepileptic drugs can also provide analgesia in fibromyalgia and neuropathic pain patients. Gabapentin and pregabalin act to reduce release of excitatory neurotransmitters (including glutamate, noradrenaline, substance P, and calcitonin gene-related peptide [52]) from nerve terminals by inhibiting the alpha-2-delta subunit of the voltage-gated calcium channel [53]. Carbamazepine is effective for trigeminal neuralgia, but not other conditions [12]. Good quality evidence demonstrates that pregabalin an effective analgesic in fibromyalgia, perhaps acting to dampen central sensitisation, but this is not clear [54].

Interventional Pain Management

The WHO pain treatment guidelines take in most of the available analgesics, however invasive procedures are not included. These include nerve block injections, denervation surgery, implantable drug delivery systems, and nerve stimulators. Invasive procedures are often risky and expensive, so they are usually reserved for cases that do not respond to oral and systemic analgesics. As these treatments have become more widely available, some authors have suggested that they be included in the pain ladder as a fourth step, coming after the strong opioids (e.g. [55, 56]). This would bring the 1986 pain ladder up to date by including more recent treatments. However, it could be argued that adding this extra step is not such a good idea: the 3-step ladder has persisted because it is simple and effective; it works because increasing the dose of a medication usually results in a reduction in pain. Adding invasive treatments as a fourth step might appear to condone the automatic use of these treatments. In cases where these treatments are unsuitable or ineffective, to use them anyway because they are the next option would be irresponsible, wasteful, and potentially harmful to patients. Leaving them out of the ladder reinforces the fact that these treatments are only suitable for use in a minority of patients, and then only after careful consideration.

Nerve block injections of steroid plus local anaesthetic into the epidural space are common for back pain, however clinical effectiveness remains debateable. In 1995 Watts and Silagy [57] published a meta-analysis concluding that epidural steroid injection was significantly more effective than placebo in providing ≥75% pain relief for up to six weeks. The number needed to treat (NNT) reveals that the level of pain relief was only achieved in 1 out of every 7 patients. McQuay and Moore [58] looked at the same data in 1998, and calculated the NNT for a more reasonable ≥50% pain relief in the short-term to be 1 in 3. Injections into facet joints of the spine are commonly used for relief of radicular pain. Evidence for efficacy is limited for cervical injections and moderate for lumbar level injections [59]. The most recent Cochrane review of this procedure concluded that there was no strong evidence for or against the use of injection therapy, but did not rule out the possibility that specific subgroups of patients may respond to a specific type of injection [60].

Surgical procedures for the treatment of chronic pain have traditionally involved the destruction of peripheral and central nerve cells in an attempt to stop ‘pain signals’ reaching the brain. Surgery is invasive, irreversible, carries a high-risk of complications, and is not always effective, therefore it is often saved until all other pharmacological and physiological treatments have been tried without success. The supposed benefits of surgery rest on the principles of the now defunct specificity theory: surgery can interrupt the ‘pain signals’ from reaching the ‘pain centre’ in the brain. This type of surgery rarely puts an end to the pain, and if successful seldom offer more than temporary relief. Despite this negative assessment, a handful of successful cases are touted as good reason to perform surgery in those who are desperate enough to believe that whatever the outcome, it is preferable to their current state of suffering. A notable exception to the high-risk/low-success surgeries is radiofrequency denervation of facet joint sensory nerves, which is moderately successful for the treatment of back and neck pain caused by nerve irritation at the facet joints of the spine. There is moderately good evidence that it provides better pain relief than sham intervention, with approximately 50% of patients reporting at least 50% pain reduction [61]. Pain typically returns 6-12 months later; however the procedure can be repeated with similar efficacy and there are no reported side effects [62].

In contrast to these destructive procedures, pain can also be treated by surgical implantation of therapeutic devices into the body. Intrathecal drug delivery systems (IDDS), first implanted in 1981 [63], use a pump

to deliver small quantities of opioid medication directly into the cerebrospinal fluid via a catheter inserted into the intrathecal space. The drug is delivered at the site of action, meaning much lower doses are needed to achieve analgesia compared with oral opioids (ratio of dose is approximately 300:1; [64]). Therefore only a small amount of drug enters the circulatory system and becomes absorbed by the rest of the body - resulting in fewer side effects and any increase in dosage will give greater analgesia relative to an increase in side effects, compared to oral opioids [65]. The evidence on IDDS for chronic non-cancer pain is currently limited to case series and a small randomised controlled trial (RCT) which supports the efficacy of intrathecal opioids in long term patients [66]. Taking also into account its invasive nature, high initial cost and risk of complications, this technology is not regularly used.

Spinal Cord Stimulation

An alternative to interrupting nerve transmission with drugs is to use electrical stimulation delivered by electrodes placed next to the spinal nerves in the dorsal epidural space. Developed as a clinical application of gate control theory [67], spinal cord stimulation (SCS) delivers an electric field to the dorsal horn and dorsal column axons, which inhibits activity in the spinothalamic tract [68]. The patient experiences paraesthesia over the area served by the SCS affected nerves, which is matched to the painful area by altering the position and settings of the electrodes during implantation. The stimulator unit is implanted subcutaneously and can be reprogrammed remotely by the physician. Recent developed rechargeable SCS devices allow the patient to recharge the unit and also increase the longevity of the device. Due to high initial cost and risk of complications, SCS is usually reserved for patients who do not respond to other less invasive forms of treatment. SCS is currently recommended by NICE in the UK for use in chronic pain of neuropathic origin continuing over six months despite standard treatments [69]. Treatment effects tend to diminish over time: in one study 67% of patients reported ≥50% reduction in pain relief lasting more than six months [70], another study 47% had ≥50% pain relief after 24 months [71]. For those patients in whom SCS is beneficial, opioid medication can be reduced, there is a significant improvement in quality of life, and side effects are rare. A recent study [72] suggested that long term efficacy of SCS is related to improvements in psychological factors including depression and autonomous coping (control over pain, ability to reduce pain, and catastrophising), although the mechanism remains unclear. Despite high initial cost and uncertainty of a successful outcome, SCS can be an effective intervention for many patients, it is reversible in the event of complications, and the treatment is performed in over 14,000 patients each year worldwide [73].

SCS has also found success in treatment of ischaemic pain arising from peripheral arterial occlusive disease (PAOD), and in the alleviation of angina pain. Extensive studies (reviewed in [74]) have revealed that SCS acts to reduce peripheral ischaemic pain by promoting the release of neuropeptides and reducing the activity of α-1 adrenergic receptors, both of which result in vasodilatation; which combines with the suppressive effect on nociceptive transmission. SCS has been shown to promote healing of ulcers [75] and reduce need for amputation in lower limb PAOD [76]. The mechanisms by which SCS acts on the heart to relieve the pain of angina have also been studied. There is no evidence that SCS works to increase coronary blood flow [77, 78], but may act to redistribute blood flow [79]; and it has been suggested that the benefit of SCS to cardiac function comes from regulation of the intrinsic cardiac nervous system [73], acting to suppress arrhythmias and attenuate ST segment elevations [74]. Systematic reviews of RCTs using SCS in the treatment of refractory angina revealed significant improvements in exercise capacity and health related quality of life for those treated with SCS [80, 81]. SCS is not currently recommended

by NICE for use in ischaemic pain conditions such as angina due to inadequate evidence [69]. To address these uncertainties, a pilot RCT compared the use of SCS to current usual care management for refractory angina [82]. A trend toward larger improvements in both primary and secondary outcomes in the SCS group was observed although the study was not formally powered to compare outcomes between the groups.

Deep Brain Stimulation (DBS)

Implantation of electrodes to stimulate brain structures involved in the transmission and regulation of nociceptive signals (the periventricular grey matter and lateral somatosensory thalamus) is a highly invasive and risky treatment method that has been in experimental use since the 1950s [83]. For these reasons DBS is only used in carefully selected patients who have not responded to all other forms of treatment, however in these few cases satisfactory and lasting pain relief has been achieved in over 50% of patients [84, 85]. DBS is approved for use in the UK for treatment of refractory chronic pain [86], in Europe for neuropathic pain [87], and is not currently approved in the USA [88].

Repetitive Transcranial Magnetic Stimulation (rTMS) and Transcranial Direct Current Stimulation (tDCS)

Non-invasive brain stimulation techniques rTMS and tDCS use equipment placed onto the scalp to induce activity in the underlying cortex via electromagnetic force (see [89] for review). Their use in pain is primarily investigational; however there is evidence for a reduction in pain when applied over the motor cortex for repeated sessions of 20 minutes or more in patients with fibromyalgia [90] and neuropathic pain [87]. Both techniques have a very few side-effects, which may include discomfort at the stimulation site and headache during stimulation, and are therefore worth trying first in patients who would otherwise undergo a surgical procedure [87].

Pain Relief by Counter-irritation

A well known phenomenon in traditional medicine, the ‘pain inhibiting pain effect’ [91] or counter-irritation [92] is the relief of pain by application of intense stimulation to the painful area or another area of the body. The mechanism of action by which pain relief is achieved depends upon the technique used.

Transcutaneous Electrical Nerve Stimulation (TENS) and Percutaneous Electrical Nerve Stimulation (PENS)

Electrical nerve stimulation via electrodes placed onto the skin (transcutaneous) or inserted into the skin (percutaneous) is used to treat a wide range of acute and chronic pain conditions, and is popular among doctors, nurses, and physiotherapists [93]. Although the use of peripheral stimulation (e.g. rubbing, vibration, heat, cold, and electrical) for pain relief has been known for thousands of years [94], an explanation for its effect was not offered until gate control theory (GCT) in 1965 [67]. Under GCT, peripheral stimulation activates large (Aβ) nerve fibres which activate spinal inhibitory neurons that attenuate small (C) fibre nociceptive activity and reduce pain. TENS has been demonstrated to inhibit nociception via this mechanism in animal and human studies [95]. Nash and colleagues [96] reported that if TENS was used for at least 30 minutes twice per day, 15% of patients achieved a 50% pain reduction

after one month, rising to 51% of patients after 24 months. McQuay and colleagues [97] concluded that TENS may be useful for chronic pain but there is no useful evidence, likely due to the fact that none of the RCTs included in the meta-analysis used anywhere near the doses of TENS recommended by the Nash study [96]. Despite lack of evidence of effect, TENS is effective for some patients and remains widely used. Evidence for efficacy of PENS is also limited, however at least one RCT has demonstrated that PENS is significantly more effective than sham intervention for short term relief of chronic pain [98].

Topical Capsaicin

Capsaicin is the compound present in chilli peppers, and can be applied externally as a cream or patch. The application of capsaicin is painful itself, therefore it was originally believed to work by distracting the patient from their pain by replacing it with another pain i.e. counter-irritation [99]. It is now known that capsaicin binds to the transient receptor potential cation channel subfamily V member 1 (TRPV1) membrane receptor, causing depolarisation and the generation of action potentials, which are felt as burning, pricking or itching sensations [100]. After repeated applications or high concentrations of capsaicin, there is a loss of normal function of the nerve cell and a persistent desensitisation to noxious stimuli, termed 'defunctionalisation' [101]. Good quality evidence of the effectiveness of capsaicin has been difficult to gather, as the burning effect of capsaicin makes blinding almost impossible. Trials confirm that high concentration capsaicin (8%) is a more effective pain reliever than lower concentrations, if the patient can overcome the initial discomfort [102], and can reduce consumption of opioid medication [103]. As topical capsaicin is relatively safe, easy to use, and has the potential to benefit some patients, it is 'worth a try' in patients who are suffering long term pain, and accounted for over 224,000 prescriptions in the UK in 2013 [104].

Heat/Cold

Superficial application of heat or cold (thermotherapy and cryotherapy, respectively) may be effective in providing immediate, short-term relief from pain [105]. Superficial heat helps to relax muscles that are tense or in spasm, and increase local circulation, thus reducing pain and stiffness [106]. Cryotherapy reduces muscular temperatures and acts to decrease local metabolism, inflammation, and pain [107]. The analgesic effect is thought to result from a decrease in nerve conduction speed and a reduction in muscle activity [108]. Heat and cold treatments are widely available, simple to use, cost effective, and patients will find out for themselves if they can benefit from them or not.

A Possible Mechanism for Counter-irritation

Experimental studies, in which brief noxious stimuli are applied to one area whilst another receives ongoing painful stimulation, shed light on a common mechanism that may subserve counter-irritation. A reduction in the activity of pain signalling neurons (in the spinal dorsal horn and trigeminal nuclei) when noxious stimuli are applied to a remote area of the body constitute a form of endogenous analgesia termed 'diffuse noxious inhibitory controls' (DNIC; [109, 110]). Although the phenomenon of DNIC has only been observed under experimental conditions, it may explain the beneficial effects of the above methods of counter-irritation which have been observed in patients.

Biopsychosocial Treatments

Up to this point, we have been discussing treatments which are essentially 'done to the patient', and thus fit into the biomedical model of pain treatment. The psychosocial health of the patient has been put to one side, perhaps with the expectation that the attenuation of pain will bring about an improvement in mental health and quality of life. However, chronic pain is as much a psychosocial problem as it is a physiological one: anxiety, depression, stress, anger, insomnia, suicide, loss of financial independence, disability, and family instability are closely associated with long-term pain. The neuromatrix theory [111] suggests that in the absence of overt physical damage, it is the psychological factors of emotion and cognition that contribute most to the experience of pain. In turn, these psychological factors are influenced by the social and cultural environment in which the patient is living, and perhaps also by side effects of pain reducing medications. The multiple aspects of the pain experience call for a complex form of treatment that can simultaneously address biological, psychological, and social issues. Such treatment draws on the knowledge of several healthcare disciplines including physicians, psychologists, specialist nurses, physiotherapists, and occupational therapists; combining to deliver what is known as multidisciplinary pain management. In a survey of chronic pain patients in 15 European countries and Israel, 23% reported they had been to see a pain management specialist [112]. In the UK, a patient will be referred by their general practitioner to the local pain clinic (of which there were 214 in 2010 [113]) for multidisciplinary treatment. On entering the pain clinic system the patient meets individually with each member of the team in order to discuss their situation and how treatment should proceed.

Physiotherapy

The goal of physiotherapy for chronic pain is to maximise and maintain the patients' functional ability, without contributing to any increase in pain. Passive modalities are less likely to be used, as they are believed to reinforce dependence on external factors when the patient should be encouraged to take responsibility for their own improvement [114]. Patients are taught that pain does not necessarily imply that tissue damage is taking place, and that avoiding activity can actually worsen pain in the long run through deconditioning. The physiotherapist may also help to validate the patient's condition, explaining that results of physical examinations, magnetic resonance imaging (MRI) scans, and other diagnostic tests often correlate poorly with pain severity and should not be relied upon as a measure of disability. Physical treatment is based on a set of stretches and light aerobic exercises performed on a daily basis, to regain muscle strength and improve range of movement that can be performed without exacerbating pain. A review of exercise therapy for chronic low-back pain concluded that it is slightly effective at decreasing pain and improving function [115].

Occupational Therapy

Occupational therapy interventions focus on increasing physical capacities, mastery of self and environment through activities, and productive and satisfying performance of life tasks and roles [116]. Patients are taught early on that rest is not a good way to deal with chronic pain, and that the performance of a baseline level of daily activity is the key to recovery. The therapist works with the patient to determine the amount of activity that can be performed without exacerbating the pain. Patients' keep a 'pain diary' noting the types of activity, duration, and pain level they experience throughout the day; which can help the patient observe what they are doing to worsen their pain. Activities are planned in advance, including regular breaks for rest – a technique known as 'pacing'. Adaptive equipment may also

be required for the patient to perform tasks, for example, a perching stool allows patients' to sit during tasks such as food preparation or washing up.

Pain Specialist Nursing

The nurse specialising in pain can advise patients on their medications, explaining the reasons why they have been prescribed, and suggesting the best time of day to take them to minimise the impact of side effects. Patients can be confused and worried when they are prescribed an antidepressant for their pain, which may lead to non-compliance; if patients understand why they are taking particular medications, they are more likely to take them [117].

Clinical Psychology

The clinical psychologist is concerned with the impact that the pain condition has on the mental health and wellbeing of the patient. Initial assessment involves psychological screening to ascertain how the pain has affected mood, sleep, appetite, motivation, daily activities, relationships, work, and finances. Patients' may be unsure why they are seeing a psychologist for pain treatment; it somehow implies that their pain is a psychological rather than a physical problem. The psychologist must take care to explain the role of non-physiological factors in the maintenance of pain symptoms and their responses to treatment [118]. Of vital importance to recovery are the ways in which the patient reacts to, and copes with physical pain and the emotional suffering that accompanies it. There are numerous approaches to psychological treatment: motivational interviewing, psychodynamic psychotherapy, operant therapy, cognitive-behavioural therapy, biofeedback, hypnosis, graded exposure, mindfulness based stress reduction, acceptance and commitment therapy, solution-focused brief therapy, and others. In a pain clinic setting, patients are often invited to attend a group therapy programme which combines elements of psychological treatment from various approaches with physiotherapy, occupational therapy, information on medication, pain physiology, sleep hygiene, local support groups, and relaxation techniques.

Patients may continue to meet regularly with team members to receive ongoing treatment and monitor progress, however it is likely that the patient will eventually be recommended to attend a series of group treatment sessions known as the pain management programme (PMP) of which there were 97 in the UK in 2013 [119], and approximately 150 in the USA in 2011 [120].

Multidisciplinary Pain Management Programmes

PMPs are based on the biopsychosocial model, in which behaviours are believed to reflect a combination of: physical events, the recognition and appraisal of these events, affective responses to these events, and environmental influences [121]. The programme addresses all of these components simultaneously. Typically, patients are treated in groups of 5-15, over a course of 8-12 sessions taking place once or twice a week on an outpatient basis. The group format normalises the experience of pain and maximises opportunities to draw on the experiences of group members; it is also cost effective ([122], p.8). Sessions last 3-4 hours and consist of physical, psychological, medical, and occupational themes. Each session will generally proceed using the same structure of five components, the contents of which change from session to session: exercise, education, skills training, relaxation, and homework. Pain management programmes

tend to differ according to the psychological approach upon which they are based, and two of these approaches will be discussed now.

Cognitive-Behavioural Therapy (CBT)

Under the cognitive-behavioural approach, individuals are not seen merely as passive responders to their environment, but as active processors of information, basing their responses on their own personal version of reality – which is constantly being revised and updated through sensory, emotional, social, environmental, and cognitive factors [123]. Over the lifetime, individuals learn ways of interpreting these factors as they are added to their version of reality, some of which may be viewed as positive, and some negative. It is the negative, or maladaptive, ways of thinking, feeling, and behaving that are the targets of CBT. Patients are taught to become aware of the connections between thoughts, feelings, and behaviours – to recognise that negative thoughts and feelings about the pain are directly linked to maladaptive behaviours and exacerbation of symptoms [124]. Unrealistic or unhelpful thoughts about pain and pain catastrophising are identified and replaced with thoughts oriented towards adaptive behaviour and positive functioning, through cognitive restructuring. Pain symptoms themselves are reconceptualised during the therapy process, with patients learning that they can control their symptoms to an extent by employing the cognitive and behavioural skills acquired during therapy [125].

The success or failure of CBT relies on the patient entering into a collaborative effort with the therapy team; they must be willing to reveal personal thoughts and feelings, and be prepared to take responsibility for their own well being by making every effort to put the skills they have learned into practice on a daily basis. It is likely that patients will initially hold the view that their pain is a medical problem and should be treated as such – by medications, manipulations, and surgery. It is therefore vital that this view is challenged at the outset, that the therapist takes time to explain the rationale of CBT, and that the patient understands their role in the treatment process. However, the patient should not be given false hope by being told that if they unquestioningly do everything asked of them, their pain will be cured, rather the patient should be encouraged to approach the therapy with a sense of sceptical optimism. A number of meta-analytic studies present convincing evidence that psychological therapies including CBT are more effective in bringing about improvements in coping and mental health than pharmaceutical treatment alone [126–130]. It should be noted that CBT does not usually bring about a reduction in pain *per se*; however this is not a goal of the treatment so it should not come as a surprise. In cases of refractory angina, a programme of education and self-management using an outpatient cognitive-behavioural programme has been successful in reducing angina symptoms. Patients attending the programme showed significant improvement on measures of angina frequency and stability, quality of life, anxiety and depression [131]; as well as a reduction in hospital visits, and a reduction in healthcare costs [132].

Acceptance and Commitment Therapy (ACT)

ACT is an approach to treatment designed around processes from the psychological flexibility model and based in operant theory and relational frame theory [133–137]. In contrast to CBT, thoughts, feelings, and behaviours are not seen as the problem which must be addressed – it is the *response* to these factors which is the target for change: it is the tendency to react in maladaptive ways and fight against the pain that causes suffering. The patient is encouraged to question whether their current courses of action are preventing them from, or helping them move towards, their life goals and values. The patient may be concerned with the eradication of pain in order to live a better life: the lack of pain is not the ultimate

goal; it is a means to an end. In chronic pain this means can never be achieved, and ACT suggests abandoning that means as it really presents a barrier to moving towards the goal of a better life [134]. ACT provides techniques that the patient can use to deal with the thoughts of pain, to minimise focus on reducing pain or thought content, engage in a process of defusing and letting go, and move towards their values and goals [134, 138]. An important technique employed to foster acceptance, to help view the self as separate from thoughts and emotions, and to aid defusion and letting go of automatic thoughts is 'mindfulness'. The essence of mindfulness is paying attention to the present moment without attaching meaning or judgmental language to thoughts that arise [139]. Seeing thoughts as transient events, separate from the self, cultivates psychological flexibility, allowing the patient to deal with difficult thoughts and feelings that might otherwise become barriers to pursuing their goals. ACT differs from CBT in the regard that it does not attempt to change thoughts and feelings: how a person has dealt with their problems in the past is not important. Patients can learn to use the skills taught in ACT to begin living a fulfilling life right away, without first *'winning a war with [their] own history'* ([134], p.652). The use of ACT as a treatment approach for chronic pain problems has grown steadily over the past 15 years. During this time evidence has accumulated that supports the use of ACT as a good alternative to CBT, with similar effects on a range of treatment outcomes [140, 141].

[Table 1 about here]

Conclusion

Pain is a multidimensional problem that must be explained and treated using a combination of biological, psychological, and social approaches (Table 1). When it comes to the treatment of chronic pain, the biopsychosocial approach provides a wider scope of inquiry and intervention than a biomedical view, and shifts the focus of the treatment away from just physical pain relief towards strategies that increase functional ability and wellbeing in spite of the pain. Such treatments are crucial in ensuring that patients maintain a satisfactory quality of life and deal with the anxiety, depression, and social upheaval which accompany persistent physical pain.

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Figure legends

Figure 1. The WHO analgesic ladder (adapted from [9], p.94).

Table Caption

Table 1. TREATMENT APPROACHES FOR CHRONIC PAIN MANAGEMENT.

Figure 1

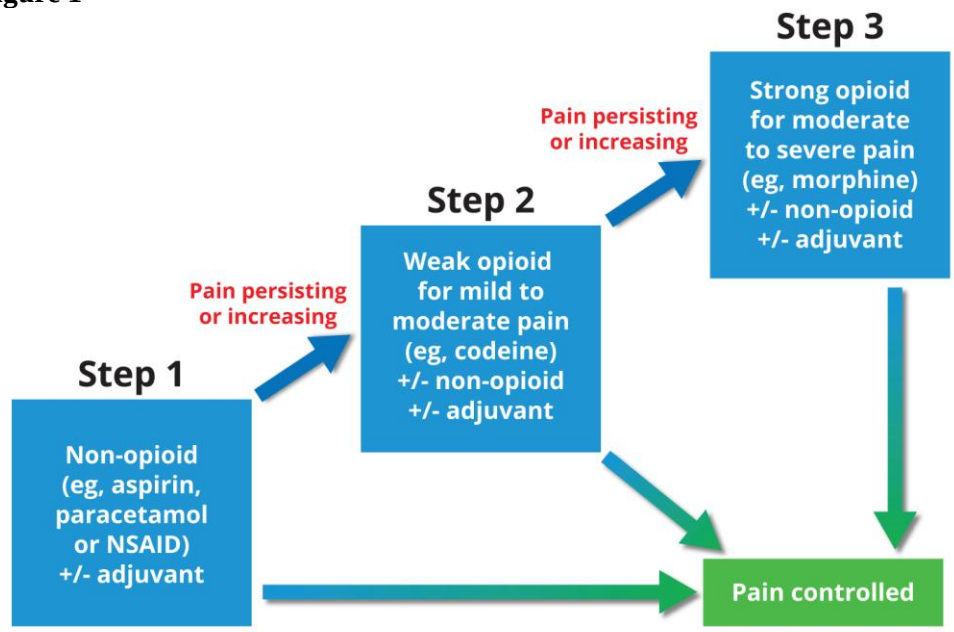

Table 1

Biomedical				Biopsychosocial
Less Invasive	Topical Analgesic	Pharmaceutical		Physiotherapy
	Oral Analgesic			
	Adjuvant Analgesic			Occupational Therapy
	Nerve Block Injection			
	Intrathecal DDS	Surgical		Specialist Nursing
	Nerve Section			
More Invasive	Deep Brain Stim.			Clinical Psychology
	Spinal Cord Stim.	Electrical		
	Percutaneous ENS			Cognitive Behavioural Therapy
	Transcutaneous ENS			
	Repetitive TMS			Acceptance and Commitment Therapy
Less Invasive	Transcranial DCS			

Abbreviations used: DDS = Drug Delivery System; Stim. = Stimulation; ENS = Electrical Nerve Stimulation; TMS = Transcranial Magnetic Stimulation; DCS = Direct Current Stimulation