Summary and Conclusions of the SBU Report on:

Methods of Treating Chronic Pain

A Systematic Review

October 2006

Project Group:
Dag Lundberg (Chair)          Eva Johansson          Björn Sjöström
Susanna Axelsson (Project Director)   Marianne Kristiansson  Åsa Svensson
Jörgen Boivie                   Thomas List                (Project Assistant)
Ingemar Eckerlund              Clas Mannheimer           Anne Söderlund
Björn Gerdle                   Lars-Åke Marké            Ania Willman
Ann-Christine Gullacksen        Gunnar L Olsson           Märta Segerdahl

Scientific Reviewers:
Harald Breivik                   Gustaf Ljungman
Eli Haugen Bunch                Ulf Persson
Jan Hasselström                 Bengt H Sjölund
Steven J Linton

English Translation:
Ken Schubert

Report: Methods of Treating Chronic Pain • Type: Systematic Review
ISBN: 91-85413-08-9, 91-85413-09-7 • ISSN: 1400-1403
Report no: 177/1+2 • Publishing year: 2006
Conclusions

How Patients Experience Chronic Pain

- The research on treating chronic pain unequivocally demonstrates a strong negative correlation between pain and quality of life, i.e., pain reduction improves quality of life (Evidence Grade 1).

- Living with chronic pain requires a new orientation in life and the opportunity to talk about the experience (Evidence Grade 2).

- Patients with chronic pain are eager to retain their sense of dignity (Evidence Grade 1).

Multimodal Rehabilitation

- The long-term impact of broad-based, coordinated rehabilitation programs, referred to as multimodal rehabilitation (usually a combination of psychological interventions and physical activity, physical exercise or physical therapy) is that pain decreases more, a greater number of people return to work and sick leaves are shorter than with passive control and/or limited, separate interventions (Evidence Grade 1). Because the studies on which that conclusion is based were structured in various different ways, any attempt to compare the magnitude of the effects may be misleading.

- Multimodal rehabilitation improves long-term functional ability in fibromyalgia patients more effectively than passive control or limited, separate interventions (Evidence Grade 2).

Cognitive Behavioral Therapy

- Cognitive behavioral therapy yields better social and physical function, as well as 25% greater ability to cope, in chronic pain patients than other behavioral therapies, medications and physical therapy that have been studied and to no treatment at all (Evidence Grade 2).

Drugs

- Paracetamol (acetaminophen) somewhat (effect size 0.21) alleviates the pain of mild to moderate osteoarthritis (Evidence Grade 1). Paracetamol is more effective in combination with tramadol or another weak opioid than as monotherapy (Evidence Grade 1).

- COX-2 inhibitors and other nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the pain of osteoarthritis and arthritis by at least 30% (Evidence Grade 1). Combining them with tramadol or another weak opioid can increase their effectiveness (Evidence Grade 1). All COX-2 inhibitors and other NSAIDs increase the risk of cardiovascular events (Evidence Grade 1). There is insufficient scientific evidence to draw any conclusions concerning possible differences between various classes of drugs.

- COX-2 inhibitors can be a cost-effective option for chronic pain patients with a high risk of gastrointestinal bleeding (Evidence Grade 2).

- Amitriptyline reduces the pain of peripheral and central neuropathic pain due to shingles (herpes zoster), diabetes and stroke patients by more than 20% (Evidence Grade 2).

- Tricyclic antidepressants moderately (effect size 0.52–0.56) alleviate fibromyalgia pain (Evidence Grade 2).

---

Effect size: <0.20: insignificant; 0.20–0.50: small; 0.50–0.80: moderate; >0.80: large. Source: Treatment of Alcohol and Drug Abuse, SBU Report 156/2, 2001, pp 403-5.
Strong opioids – number needed to treat (NNT)² approximately 2.6 – alleviate neuropathic pain in diabetes and shingles patients (Evidence Grade 1). Strong opioids reduce severe osteoarthritis pain by approximately 2.4% (Evidence Grade 1). Weak opioids reduce mild to moderate osteoarthritis and low back pain by approximately 40% (Evidence Grade 1). They are just as effective as NSAIDs for osteoarthritis pain (Evidence Grade 1). Both weak and strong opioids cause unpleasant adverse effects (the most common of which are constipation, fatigue, dizziness, nausea and vomiting) in more than half of all patients (Evidence Grade 1).

Carbamazepine is effective (NNT 1.4–2.8) in trigeminal neuralgia (tic douloureux) (Evidence Grade 2). Gabapentin (Neurontin) reduces neuropathic pain (NNT 3.8 for at least 50%) in diabetes (Evidence Grade 2) and in patients with postherpetic (NNT 3.2) pain (Evidence Grade 1).

Tramadol is more effective than placebo for nociceptive pain – approximately 20% of tramadol patients, as opposed to 40% of placebo patients, stop taking their medication due to insufficient relief (Evidence Grade 1). Tramadol alleviates neuropathic pain (NNT 4.3 for at least 50% pain relief) (Evidence Grade 3). Tramadol is as effective as weak opioids for musculoskeletal pain (Evidence Grade 1). Tramadol causes adverse effects to the same extent as weak and strong opioids (Evidence Grade 1).

Capsaicin reduces (NNT 8 for at least 50%) neuropathic pain and osteoarthritis pain in small joint pain (Evidence Grade 1).

The research results are contradictory when it comes to the effectiveness of glucosamine in relieving osteoarthritis pain.

² Number of patients who must be treated before one of them is likely to benefit. The lower, the better.

Medical Instruments
- Spinal cord stimulation reduces the frequency of angina attacks by 50% and improves quality of life, both short-term and long-term, in patients with severe angina pectoris or the ischemic symptoms of peripheral arterial disease (Evidence Grade 1).

- Radiofrequency denervation (Evidence Grade 3) can provide short-term relief of chronic neck and back (including whiplash-related) pain but poses a risk of serious complications.

Physical Activity, Physical Exercise, Relaxation, Biofeedback, Massage, Manipulation, Physical Therapy and Orthosis
- Active, specific and professionally supervised exercise alleviates chronic pain 20–30% more effectively than treatment that does not involve physical activity (Evidence Grade 1).

- Treatment strategies that include physical activity are more cost-effective in alleviating chronic low back pain than standard primary care, that does not involve specific measures (Evidence Grade 3).

Acupuncture
- Western acupuncture alleviates chronic low back pain more effectively than placebo (Evidence Grade 1).

- There is strong scientific evidence that acupuncture alleviates low back pain, lateral epicondylitis (tennis elbow), neck and shoulder pain as effectively as other treatments (Evidence Grade 1).
Other Methods

- Balneotherapy (mud or mineral baths) reduces chronic musculoskeletal pain by 20–30% (Evidence Grade 3).

Odontological Methods

- In orofacial pain, occlusal splints and behavioral therapies such as biofeedback and cognitive behavioral therapy give better pain relief than no therapy at all (Evidence Grade 3).

Chronic Pain in Children

- Psychological methods (NNT 2.35) alleviate tension (muscle contraction) headaches in children more effectively than placebo, standard primary care (which does not involve specific measures) or no treatment at all (Evidence Grade 1).

Fact box 1. Study Quality and Relevance, Evidence Grade.

- Study quality and relevance refers to the scientific quality of a particular study and its ability to reliably address a specific question.

- Evidence Grade refers to the total scientific evidence for a conclusion, i.e., how many high-quality studies support the conclusion.

Evidence Grade 1 – Strong Scientific Evidence

A conclusion assigned Evidence Grade 1 is supported by at least two studies with high study quality and relevance among the total scientific evidence. If some studies are at variance with the conclusion, the Evidence Grade may be lower.

Evidence Grade 2 – Moderately Strong Scientific Evidence

A conclusion assigned Evidence Grade 2 is supported by at least one study with high study quality and relevance, as well as two studies with medium study quality and relevance, among the total scientific evidence. If some studies are at variance with the conclusion, the Evidence Grade may be lower.

Evidence Grade 3 – Limited Scientific Evidence

A conclusion assigned Evidence Grade 3 is supported by at least two studies with medium study quality and relevance among the total scientific evidence. If some studies are at variance with the conclusion, the Evidence Grade may be lower.

Insufficient Scientific Evidence

If no studies meet the study quality and relevance criteria, the scientific evidence is rated as insufficient to draw any conclusions.

Contradictory Scientific Evidence

If different studies are characterized by equal study quality and relevance but generate conflicting results, the scientific evidence is rated as contradictory and no conclusions can be drawn.
Background

The experience of pain is associated with emotional and psychological reactions that cannot be objectively measured. Pain is referred to as chronic only when it has lasted for a certain period of time, ordinarily three months. Pain that has persisted that long is often accompanied by other symptoms, such as limitations and difficulties in day-to-day living.

Approximately 20% of the population, a significant number of which has trouble coping, suffers from moderate to severe chronic pain at any particular time. Many of them are on sick leave and/or receiving some kind of treatment. The socioeconomic cost of chronic pain among Swedes totaled an estimated SEK 87.5 billion in 2003. Direct, care-related costs accounted for SEK 7.5 billion of the total, while indirect costs – loss of production due to sick leave – accounted for SEK 80 billion.

Chronic pain is not synonymous with acute pain over an extended period of time. It is partially a manifestation of permanent changes both to the neural pathways that transmit pain and to other tissues. Chronic pain is regarded as a special condition in which the original cause is of minor importance and often plays no role at all in determining the appropriate treatment. Nevertheless, both diagnostic and treatment considerations may occasionally justify an attempt to categorize chronic pain as either nociceptive (due to tissue damage), neuropathic (due to injury to the nervous system), somatoform (due largely to psychological factors) or unknown in origin. Psychological factors also affect the experience.
and behavior of people with chronic pain. A high degree of comorbidity has been found between chronic pain and various types of psychological problems. There is much to indicate that the depression that often occurs simultaneously with chronic pain is the result rather than the cause. Chronic pain should be seen as neither a wholly biomedical phenomenon nor the sole result of psychological difficulties or conditions. The biopsychosocial model attempts to integrate the mind–body complex and observe chronic pain from a multifactorial point of view.

This report presents the results of a systematic review of the scientific literature on methods for treating chronic pain conditions. The review proceeded from the following questions:

• What methods are effective for treating patients with chronic pain conditions?
• What is it like to live with chronic pain and how is day-to-day living affected?
• What health economic considerations are involved in treating patients with chronic pain conditions?

Methodology

The Project Group’s Mission

Electronic database searches identified the scientific evidence for addressing the above questions. Predetermined inclusion criteria limited the searches. Treatment of cancer, migraine, vaginal and chest pain, other than angina pectoris, was not included. The review of multimodal rehabilitation did not look at rheumatoid arthritis. The project did not include surgical procedures, with the exception of certain neurosurgical interventions, methods in the experimental stage and measures for dealing with a presumed cause of the pain condition, such as anti-inflammatory treatment of inflammatory diseases. If a previous systematic overview addressed a particular question, the search was limited to the years following the period that it had covered. The search otherwise focused on recent studies, primarily those published after 1990.

The report also includes a review of methods referred to as alternative or complementary. These methods, which are not generally accepted and/or have not been integrated into standard medical practice, vary from one cultural and regional tradition to the next. They are described as complementary when used in addition to, and alternative when used in place of, standard procedures.

The scientific evidence for treating chronic face and jaw pain is described in a separate chapter, as is treatment of pain in children. The reason for the decision to discuss the two areas separately is that they involve special groups of caregivers and patients.

Search and Review of the Literature

Relevant literature was sought in the Medline, Cochrane Library, Cinahl and PsycInfo databases. An initial selection of studies was made by reviewing the extent to which the summaries identified by the database searches met the predetermined inclusion criteria. The next step involved ordering complete articles. The studies that met the inclusion criteria were reviewed in terms of study quality and relevance, i.e., the degree to which they addressed the project’s questions, how well they were conducted and how reliable their results were deemed to be. Each study was rated as having high, medium or low study quality and relevance. Only studies with high or medium study quality and relevance formed the basis of the project’s conclusions.

Qualitative studies were subjected to a more classic, inductive review. Based on predetermined criteria, each article was assessed in accordance with the protocol. Only high-quality or medium-quality studies that were either phenomenological or employed grounded theory were included.
Multimodal Rehabilitation

Multimodal rehabilitation (broad-based, coordinated rehabilitation programs) involves interventions that proceed from a holistic perspective, integrating medical and social measures that reflect the patient’s particular needs and situation in the community. A general objective of multimodal rehabilitation is to alleviate pain while improving the patient’s ability to function and work. Based on the biopsychosocial model, multimodal rehabilitation of patients with chronic pain conditions may include various combinations of physiotherapeutic, social, educational, psychological, etc., interventions. The rehabilitation programs often reflect the available specialist expertise. An multidisciplinary team may consist of a doctor, physical therapist, social worker, occupational therapist, psychologist and nurse who jointly design a specific program on the basis of the particular expertise that they possess.

Studies of multimodal rehabilitation frequently compare it with more passive treatment. The control group may be made up of patients on a waiting list who are offered the same treatment several months later. The results of rehabilitation are measured in a number of different ways. How patients rate the intensity of their pain is almost always part of the studies included by this project.

Results

The Experience of Living with Chronic Pain

People with chronic pain tend to focus their attention on their discomfort and on what they perceive as being unknown or abnormal about their bodies. The pain often governs their lives and interferes with their daily activities. Fatigue and sleep disturbances are common. People with chronic pain seek relief, either through medication or more active or invasive measures. In order to cope better, they also look for a diagnosis or generally accepted explanation for their pain.

Chronic pain has social and psychological consequences as well. Many patients feel trapped, as though they have lost their sense of dignity. One common pattern is to alternate between strong feelings of hope and despair.
Multimodal rehabilitation that combines psychological interventions (such as cognitive behavioral therapy) with measures aimed at improving physical functioning generates better long-term results in treating chronic pain than less comprehensive methods (Evidence Grade 1). The effect can be measured as return to work or reduced sick leave. Multimodal rehabilitation more effectively improves functional ability in fibromyalgia patients than less comprehensive methods (Evidence Grade 2). Multimodal rehabilitation is more cost-effective than standard treatment of chronic low back pain (Evidence Grade 3).

**Psychological Methods**

Cognitive behavioral therapy (CBT) focuses on actively influencing the patient’s behavior by changing dysfunctional and counterproductive thought patterns. The goal is to increase the patient’s ability to cope with the difficulties related to the disease and instill a greater sense of control. Instructional methods strive to cultivate a new, more productive perspective on the disease.

Many studies or psychological methods rate not only pain intensity, but also the patient’s ability to function and cope. But because the effectiveness of CBT is measured so differently from study to study, this project performed an overall global assessment of the results. The control groups are often made up of patients on a waiting list.

The review demonstrated that CBT is more effective for chronic pain than other types of behavioral therapy, medication or physical therapy (Evidence Grade 2).

**Drugs**

The most common medications for treating chronic pain conditions are paracetamol (acetaminophen), nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, opioids, tramadol and anticonvulsants.

Only a handful of drug classes have been developed for the specific purpose of treating chronic pain. Many of the medications currently used for chronic pain have been approved for other indications. The fact that the pure pharmacological effect of a drug for treating chronic pain is often demonstrable after 5–6 half-lives may impact the assessment of its value. Because drug trials are of relatively short duration, they are unable to determine whether the medication has subsequent adverse effects on chronic treatment or leads to dependence/abuse.

**Paracetamol**

Paracetamol is a common drug for chronic pain, such as that associated with osteoarthritis. Paracetamol offers some relief to osteoarthritis patients (Evidence Grade 1). It is less effective than NSAIDs (Evidence Grade 1). Paracetamol is also effective for tension (muscle contraction) headaches (Evidence Grade 3). If the drug is taken in the proper dosage, the reported adverse effects have not been shown to be greater than placebo (Evidence Grade 1). Overdoses pose a risk of hepatotoxicity (liver toxicity).

**Anti-inflammatory Drugs**

NSAIDs have been used to treat pain ever since the 1970s. They appear to act both peripherally in the tissues and in the central nervous system. NSAIDs can cause adverse effects in the gastrointestinal tract, the most serious of which is frank bleeding. Given that the risk of adverse effects is significantly greater for the highest dose interval, the lowest effective dosage is desirable.

NSAIDs have been improved with the goal of minimizing the most serious adverse effects while retaining or increasing their analgesic and anti-inflammatory properties. The COX-2 inhibitors are one result of that effort.
NSAIDs are more effective than placebo for osteoarthritis (Evidence Grade 1) and low back (Evidence Grade 2) pain. There is limited scientific evidence that NSAIDs are more effective than placebo and paracetamol for tension (muscle contraction) headaches (Evidence Grade 3). The various NSAIDs and COX-2 inhibitors are equally effective in relieving osteoarthritis and rheumatoid arthritis pain (Evidence Grade 1). If the recommended dosage is insufficiently effective, a weak opioid or tramadol supplement can provide added pain relief. Topical application of NSAIDs reduces chronic musculoskeletal pain more effectively than placebo (Evidence Grade 3).

Although long-term use of NSAIDs increases the risk of cardiovascular disease (Evidence Grade 1), the scientific evidence is insufficient to conclude whether there are any differences among various classes of drugs. COX-2 inhibitors can be a cost-effective option for chronic pain patients with a high risk of gastrointestinal bleeding (Evidence Grade 2).

Antidepressants

It has since long been known that antidepressants affect the central norepinephreric systems, thereby offering the potential to modulate pain. As a result, various types of antidepressants have been tried for a number of different chronic pain conditions. Antidepressants vary with respect to their mode of action. The psychiatric profession has largely replaced the older tetracyclic and tricyclic antidepressants with the newer selective serotonin (SSRIs) and noradrenaline (SNRIs) reuptake inhibitors. The studies reviewed by this project examined all types of pain, from the nervous system, fibromyalgia, tension (muscle contraction) headaches and low back. The drug dosages varied. Because the medications are metabolized differently from one person to the next, it is difficult to determine whether the dose regimen influences effectiveness.

Tricyclic antidepressants can alleviate chronic tension (muscle contraction) headache (Evidence Grade 1), peripheral and central neuropathic, fibromyalgia (Evidence Grade 2) and low back (Evidence Grade 3) pain. The scientific evidence does not permit any conclusions concerning the effectiveness of SSRIs or SNRIs in treating chronic pain conditions. Tricyclic antidepressants often cause adverse effects such as xerostomia (dry mouth) and dizziness.

Opioids

Concern about the potential for abuse has limited the prescription of opioids for patients with chronic pain unrelated to cancer. No increased risk of dependence/abuse has been detected during the short periods, usually no longer than six months, that studies have followed patients. Because the studies exclude subjects who are known to have had previous substance abuse problems or are at risk to have dependence tendencies, it is difficult to assess the risk of prescribing opioids in clinical practice.

The use of weak opioids (codeine and dextropropoxyphene) for osteoarthritis pain is largely undisputed. But prescribing strong opioids (morphine, oxycodone and fentanyl) for chronic pain is a matter of controversy given their uncertain effectiveness, adverse effects and potential for dependence/abuse. The following conclu-
Tramadol has a weak opioid, as well as an SSRI, effect. Prescribers of tramadol must pay attention to a number of pharmacokinetic and pharmacodynamic interactions. Use of the drug can lead to dependence/abuse.

Tramadol in combination with paracetamol alleviates nociceptive pain more effectively than placebo (Evidence Grade 1).

Tramadol is more effective than placebo for neuropathic pain (Evidence Grade 3). More than half of study subjects experience adverse effects, usually nausea, fatigue, dizziness, constipation, sweating, dry mouth, itching, headache and vomiting. There is also a risk of allergic and other serious hypersensitivity reactions.

Capsaicin

Capsaicin releases substance P and calcitonin gene-related peptide from the peripheral endings of primary afferent fibers that are responsible for pain pathways. In addition, the perfusion of blood in the tissues increases. Because the treatment is topical, no general adverse effects or drug interactions occur. The patient may feel a temporary burning sensation in the skin at the site where the medication is applied.

Topical application of capsaicin alleviates neuropathic and small joint pain (Evidence Grade 1). There is insufficient scientific evidence to draw any conclusions about the effectiveness of capsaicin for other chronic pain conditions.

Other Analgesics

The medications mentioned above fail to provide pain relief for a considerable percentage of chronic pain patients. As a result, attempts have been made with treatment using other types of drugs. Clinical studies that met the inclusion criteria for this systematic review examined the effectiveness of NMDA-receptor antagonists, clonidine, mexiletine, cannabinoids, glucosamine,
chondroitin sulfate, sympathetic blockades and injections of local anesthetics, as well as local injections of steroids and botulinum toxin.

Cannabinoids alleviate central neuropathic pain (Evidence Grade 1). High doses of chondroitin sulfate (800–1200 mg daily) are somewhat effective in alleviating osteoarthritis pain (Evidence Grade 1). None of the studies identified by the project demonstrated any analgesic effects of clonidine for diabetic polyneuropathy (Evidence Grade 3), mexiletine for neuropathic pain (Evidence Grade 1) or spinal steroid injections for chronic back pain (Evidence Grade 1). Single injections of botulinum toxin have no analgesic effect for either musculoskeletal pain or tension (muscle contraction) headache (Evidence Grade 2). The scientific evidence does not permit any conclusions concerning the effectiveness of any of the other medications mentioned above.

**Invasive Therapies**

*Spinal Cord Stimulation*

Implanted spinal cord stimulators have been used in the treatment of chronic pain conditions since the 1960s. Electrical stimulation of the dorsal longitudinal bundles is based on the gate control theory of pain. Spinal cord stimulation is used for refractory angina pectoris, as well as peripheral ischemic (poor blood circulation in the legs), neuropathic and low back pain.

Spinal cord stimulation is effective long-term for alleviating the pain and improving the quality of life in patients with refractory angina pectoris (Evidence Grade 1) and alleviating peripheral ischemic pain (Evidence Grade 1). The method has been shown to reduce peripheral neuropathic (Evidence Grade 3) and low back (Evidence Grade 2) pain. Notwithstanding high initial expenses, spinal cord stimulation combined with physical therapy is cost-effective in treating neuropathic pain and angina pectoris (Evidence Grade 3).

*Radiofrequency Denervation*

Radiofrequency denervation involves inserting a needle under the skin into a sensory nerve. An inner cannula (catheter-like device) permits the passage of high-frequency electrical current. The current damages the nerve fibers, some of which degenerate. Initial use of a new radiofrequency denervation method, regarded as less damaging to the tissues, has generated no scientific evidence from which to assess its effectiveness.

Radiofrequency denervation has a short-term (up to one year) analgesic effect for neck and back (including whiplash-related) pain (Evidence Grade 3) but poses a risk of serious complications. There is no scientific evidence for drawing any conclusions about its long-term effects.

Radiofrequency denervation is an invasive method that poses the risk of serious complications, including arterial puncture, venepuncture, nerve damage, postoperative pain, bleeding and infections.

*Deep Brain Stimulation*

This method uses electrodes that have been placed into the brain. The stimulation is alleged to increase the quantity of endogenous opioids in the cerebrospinal fluid. Studies attempting to distinguish the results from placebo effect suggest that the treatment offers small but significant benefits. Follow-up studies show that the method provides pain relief for certain well-selected patients.
Deep brain stimulation is an option when other approaches have proven ineffective in alleviating chronic pain. Due to ethical considerations, treatment studies that would yield unambiguous and statistically reliable results cannot be conducted.

**Motor Cortex Stimulation**

This method involves using a pulse generator to stimulate one or more electrodes that have been permanently implanted on the surface of the brain. The patient can regulate the intensity of the stimulation. Central neuropathic pain and peripheral neuropathic pain from the head and neck region are the most common indications for this method.

All studies reviewed by this project were follow-ups that performed measurements before and after treatment. Approximately half of the patients appeared to have experienced pain relief up to six years after implantation. But the scientific evidence was insufficient to draw statistically reliable conclusions.

**Nerve Lesioning**

During the 1970s, treatment of chronic and severe neuropathic pain was largely based on neurosurgical procedures. The purpose was to structurally damage specific nerves, neuron clusters or neural pathways. Since these treatments can lead to severe complications, including neurological deficit and increased pain, they are, with occasional exceptions no longer used in Sweden. It goes without saying that the methods are unsuitable for comparative, controlled studies. The incomplete information available is based on follow-up studies, case reports and the narratives of surgeons. The long-term effectiveness of the treatments are shown to be limited. A neurosurgical procedure still used in Sweden is called dorsal root entry zone (DREZ) lesioning. This particular method also carries the risk of severe adverse effects and has failed to demonstrate satisfactory long-term results.
scientific evidence to draw any conclusions about the effectiveness of exercise for reducing fibromyalgia pain.

Relaxation and Biofeedback
Relaxation can be supervised by a therapist or done at home on the basis of instructions, sometimes recorded. During biofeedback, patients become aware of tension in their muscles. The idea is to make it easier to learn an effective relaxation technique. The theory of relaxation, with or without biofeedback, is that reduced muscle tension alleviates pain.

When it comes to the relative effectiveness of relaxation and other methods, the scientific evidence is contradictory. There is insufficient evidence to draw any conclusions about the effectiveness of biofeedback.

Massage
The scientific evidence is insufficient to draw any conclusions about the analgesic effect of massage.

Manipulation/Mobilization
Orthopedic manual therapy (OMT) may involve measures – including soft tissue therapy, stretching, mobilization, manipulation and stabilization exercises – that relieve pain, increase movement and improve stability. The therapy consists of slow, passive movements. A short active movement at the end trajectory may be included. The studies reviewed by the project often combined manipulation/mobilization with exercise or passive treatment (massage or heat).

The scientific evidence is contradictory with regard to the relative effectiveness of manipulation/mobilization and other methods.
Acupuncture are complex. Biological control systems may be intertwined at various levels, and our knowledge of how they interact is limited.

Acupuncture is more effective than no treatment at all in alleviating neck, shoulder and chronic low back pain (Evidence Grade 1). Acupuncture alleviates lateral epicondylitis (tennis elbow) pain more effectively than laser therapy or placebo (Evidence Grade 1). Real acupuncture is more effective than placebo acupuncture in alleviating low back pain (Evidence Grade 1), as well as more effective than no treatment at all for face and whiplash-related pain (Evidence Grade 3). The adverse effects of active acupuncture – fatigue, nausea and more intense pain – are mild and transient.

Alternative and Complementary Methods

Many people who suffer from ailments that are not easily cured by conventional treatments of modern health care, eg chronic pain, instead often turn to alternative treatments. These include other treatment methods and life style related activities. The therapies are often based on a holistic philosophy of life, in accordance with which the body and spirit cannot be treated separately. Patients, more often women than men, frequently pay out of their own pockets.

Patients with chronic muscle and joint pain obtain more immediate and long-term relief (Evidence Grade 3) from balneotherapy (mud or mineral baths) at spas than spa visitors who do not receive any specific bath therapy.

Individualized homeopathy is no more effective than placebo for chronic pain conditions (Evidence Grade 1). Ginger, avocado and soybean extract, as well as rosehips powder, is more effective than placebo in alleviating osteoarthritis pain (Evidence Grade 3).
Studies that have examined the effectiveness of Tai Chi, Qigong, yoga, hypnosis, mindfulness meditation, music, Snoezelen, subcutaneous carbon dioxide injections, stinging nettle, e-mail counseling, natural healing, other herbs and nutritional supplements are too few and diverse to permit any conclusions.

**Treating Chronic Face and Jaw Pain**

A common chronic condition, pain in the jaw system can proceed from any of its parts. The source of temporomandibular dysfunction (TMD) remains uncertain. Dysfunction, stress and other emotional stimuli have all been regarded as causing pain as the result of increased facial muscle tonus, reduced circulation in the tissue or inflammation. Whether such pain conditions are accompanied by tissue damage remains unclear. The treatment focuses on normalizing jaw function by reducing bite disturbances or imbalances, etc, or on directly alleviating pain by means of various methods.

In orofacial pain, occlusal splints and behavioral therapies such as biofeedback, cognitive behavioral therapy give better pain relief than no therapy at all (Evidence Grade 3).

Specific pharmacological methods for chronic face and jaw pain have yielded contradictory results. Adverse effects are common.

**Treating Chronic Pain Conditions in Children**

Studies show that approximately one in four schoolchildren report chronic or recurrent pain conditions. The condition is commonly limited to the head, arms, legs or abdomen – such as Recurrent Abdominal Pain Syndrome (RAPS). Our knowledge about neuropathic pain in children is scanty. Complex Regional Pain Disorder, which mainly affects girls, may be related to stress.
Phantom pain is common after amputation of a child’s limb, as well as in amelia (congenital absence of an arm or leg). Fibromyalgia, whiplash-related pain conditions and low back pain, which are common among adults, also occur in children but are diagnosed less often.

Controlled studies that examine the treatment of chronic pain conditions in children are rare. This project identified studies that looked at the effectiveness of psychological methods, cognitive behavioral therapy, drugs, physical therapy, dietary treatment, occlusal splints and various stimulation techniques.

Psychological methods, relaxation and biofeedback effectively alleviate tension (muscle contraction) headaches in children (Evidence Grade 1). Dietary treatment has no impact on RAPS (Evidence Grade 3). The scientific evidence is insufficient to draw any conclusions about the other methods.

**Ethical Aspects of Treating Chronic Pain Conditions**

The scientific literature on which this report is based usually looked only briefly and generally at the issue of ethics – whether in research or in the treatment and care offered by the healthcare system.

The tradeoff between benefit and risk must be weighed carefully every time a potentially dangerous measure is prescribed. The principle should be taken into account when considering the use of approaches – such as many of the high-tech invasive methods described in this report – that have potential adverse effects and for which the scientific evidence of benefit is contradictory or insufficient.

For various reasons, patients with chronic pain accompanied by psychological and social complications represent a group that is at risk of being discriminated against and accorded low priority. The fear of dependence/abuse may make doctors reluctant to prescribe morphine formulations, even for severe chronic pain. As a result, patients may not have access to the pain relief that they need. Patients with a known history of substance abuse are particularly at risk of being discriminated against in this respect. However, substance abusers who simulate pain can take up healthcare time and resources that would be more appropriately devoted to other patients.

Studies of various methods for treating chronic pain often exclude patients with impaired decision making abilities or difficulty communicating with others. Thus, the results of such studies cannot be generalized as much as they could be otherwise.

One problem for studies of chronic pain treatment is that ethical considerations limit their length. Otherwise, the control subjects would be at risk of suffering from untreated or poorly treated pain. Short study periods eliminate the opportunity to check for late adverse affects or therapy failure due to drug intolerance. Thus, drug trials with short treatment periods can be unethical in that they contribute to the use of medications with a high risk/benefit ratio.

Psychological and social problems often develop when pain becomes chronic and appears difficult to treat. The doctor/patient relationship may deteriorate – for instance, patients may withhold information concerning alternative methods that they are using, or doctors may take insufficient interest in what patients are experiencing. Patient and doctor autonomy may clash, making it more difficult to maintain proper care and optimal treatment.

**Future Research**

There are significant gaps in our knowledge concerning the effects of various methods for treating chronic pain conditions. This project has identified the following areas as particularly important:

- There is a lack of safe, effective drugs for treating chronic pain conditions.
• In-depth knowledge of long-term effects is lacking for all chronic pain treatments examined by this project. When it comes to drug trials, open follow-up studies (preferably multi-year) can contribute to our knowledge of long-term effects, as well as dependence/abuse and adverse effect issues.

• The availability of studies regarding the impact and cost-effectiveness of various methods on quality of life is highly limited. Such information is especially crucial for treating chronic pain conditions that may persist for an extended period of time.

• Because uncertainty as to the outcome measures used to assess the effectiveness of treatment makes the studies difficult to compare, future research needs to be more uniform with respect to the methods by which it evaluates function, social rehabilitation, etc.

• To increase our knowledge concerning the effects of psychological approaches, the context and circumstances (not simply the method) in which treatment is provided should be described in greater depth – for instance, the significance of the interaction between the therapist and patient can be explored.

• More knowledge is needed regarding the role of the patient in the treatment of chronic pain. The approach of continually activating the patient while the therapist serves as motivator and counselor may turn out to affect the outcome of treatment. Chronic pain patients are often relegated to a passive role that may contribute to locking them into the healthcare system, thus leading to iatrogenic (physician-induced) injuries. Our knowledge is limited when it comes to how information and instruction should be used, as well as how compliance with various treatment regimens can be improved, particularly by means of exercise and home rehabilitation programs.

• More studies, both qualitative and quantitative, are needed that examine chronic pain from psychological and social points of view. Research is lacking about the possible value of tailoring special rehabilitation measures to particular groups of patients, such as men, women, children, immigrants, refugees, the elderly and people with cognitive disorders. The significance of the setting in which care is provided (including how it is organized) should be explored on the basis of what the patient experiences, what results treatment achieves and what health economic considerations come into play.
### Table A Overview of effective treatments for various pain conditions.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment that is effective for pain</th>
<th>Evidence grade</th>
<th>Chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina pectoris (refractory)</td>
<td>Spinal cord stimulation (SCS)</td>
<td>1</td>
<td>8.1</td>
</tr>
<tr>
<td>Central neuropathic pain</td>
<td>Amitriptyline</td>
<td>2</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>Cannabisoids</td>
<td>1</td>
<td>7.9</td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>NSAIDs</td>
<td>2</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>Specific exercise</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Exercise, including components that affect behavior</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Multimodal rehabilitation, including psychological methods</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants</td>
<td>3</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>Weak opioids</td>
<td>1</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Spinal cord stimulation (SCS)</td>
<td>2</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>Behavioral therapy</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Acupuncture</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Harpago (herb)</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Chronic neck pain</td>
<td>Acupuncture</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Supervised exercise</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Exercise, including components that affect behavior</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Multimodal rehabilitation</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants</td>
<td>2</td>
<td>7.3</td>
</tr>
<tr>
<td>Knee joint pain</td>
<td>Eccentric exercise</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Lateral epicondylitis (tennis elbow)</td>
<td>Acupuncture</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>Strong opioids</td>
<td>2</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Balneotherapy (mud or mineral baths)</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>Anticonvulsants</td>
<td>1</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>Tramadol</td>
<td>3</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>Topical capsicin</td>
<td>1</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td>Amitriptyline</td>
<td>2</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>Strong opioids</td>
<td>1</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Spinal cord stimulation (SCS)</td>
<td>3</td>
<td>8.1</td>
</tr>
<tr>
<td>Diabetic polyneuropathy</td>
<td>Amitriptyline</td>
<td>2</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>Strong opioids</td>
<td>1</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Gabapentin</td>
<td>2</td>
<td>7.5</td>
</tr>
<tr>
<td>Postherpetic neuralgia</td>
<td>Amitriptyline</td>
<td>2</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>Gabapentin, pregabalin</td>
<td>1</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>Strong opioids</td>
<td>1</td>
<td>7.4</td>
</tr>
</tbody>
</table>

### Condition | Treatment that is effective for pain                                      | Evidence grade | Chapter |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>Nonsteroidal anti-inflammatory drugs (NSAIDs)/ COX-2 inhibitors</td>
<td>1</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>Paracetamol</td>
<td>1</td>
<td>7.1</td>
</tr>
<tr>
<td></td>
<td>Topical capsicin in the small joints</td>
<td>1</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td>Strong and weak opioids</td>
<td>1</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Avocado/soybean extract</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Chondroitin sulfate</td>
<td>1</td>
<td>7.9</td>
</tr>
<tr>
<td>Knee osteoarthritis</td>
<td>Strength and flexibility training</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>(see Osteoarthritis)</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Peripheral ischemic pain</td>
<td>Spinal cord stimulation (SCS)</td>
<td>1</td>
<td>8.1</td>
</tr>
<tr>
<td>Rheumatoid arthritis*</td>
<td>NSAIDs</td>
<td>1</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>Topical capsicin in the small joints</td>
<td>1</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td>Warm paraffin on the hands combined with exercise</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Temporo-mandibular dysfunction (TMD)</td>
<td>Acupuncture</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Occlusal splints</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Methods that affect behavior (biofeedback, cognitive behavioral therapy)</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Tension (muscle contraction) headache</td>
<td>NSAIDs are more effective than placebo and paracetamol</td>
<td>3</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>Paracetamol</td>
<td>3</td>
<td>7.1</td>
</tr>
<tr>
<td></td>
<td>Amitriptyline</td>
<td>1</td>
<td>7.3</td>
</tr>
<tr>
<td>Trigeminal neuralgia</td>
<td>Carbamazepine</td>
<td>2</td>
<td>7.5</td>
</tr>
<tr>
<td>Whiplash-related pain</td>
<td>Acupuncture</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Radio frequency denervation</td>
<td>3</td>
<td>8.2</td>
</tr>
</tbody>
</table>

*The review of multimodal rehabilitation did not look at rheumatoid arthritis.

Evidence grade:
1 = Strong scientific evidence
2 = Moderately strong scientific evidence
3 = Limited scientific evidence.