What the Research Evidence actually tells us

There are some problems with the evidence that we have for some treatments. Often problems occur when rolling out a trial e.g. they're too short, small, using biased methods so the validity of the results is questionable.

Green indicates good evidence base, amber indicates some evidence and Red indicates no evidence.

Treatment	How we think It works	Positive	Negative	Recommendations	Have you tried this? What was your experience?
Paracetamol	Blocks the production of prostaglandins, chemicals that are produced by your body in response to illness or injury. It makes the body less aware of the pain.	Few side effects	Liver toxicity in high doses	A review in Cochrane in December 2016 showed paracetamol provides minimal short term benefit for osteoarthritis. That it's no better than placebo in acute low back pain and uncertain effect in chronic low back pain. In 2017 a Cochrane review looked at the combination of paracetamol with codeine and dihydrocodeine which again showed little benefit. There is insufficient evidence to support or refute the suggestion that paracetamol alone or in combination has any efficacy in Chronic non cancer pain (CNCP).	

Opiates	They bind to and block certain danger receptors located peripherally and centrally, stopping danger messages going down nerves.	Short term can help reduce acute pain but be limited to the lowest dose for the shortest period to achieve adequate pain relief. The risk of longer term use in the intractable pain of cancer is more acceptable. There is evidence to show opioids are underused for such patients. They can also help with cough and diarrhoea.	Using long term can lead to need for escalated doses because of loss of effectiveness (tolerance), addiction and increased pain levels. There is increasing evidence for inappropriate over prescribing for non-cancer pain. Side effects include drowsiness, constipation, nausea and vomiting, medication overuse headache, dry mouth, sweating, restlessness, confusion, hallucinations, Dizziness, respiratory depression. If you become dependent withdrawal effects can include body aches, diarrhoea, loss of appetite, cramps, insomnia, sweating, yawning, irritability.	There is insufficient evidence to support or refute the use of opiates and in the absence of any supporting evidence they should probably not be recommended. In October 2017 Cochrane found no evidence for the use of high dose opiates in CNCP.	

Cannabis-based products - herbal, plant-derived, synthetic.	The cannabinoid system has multiple functions that move the organism back to equilibrium. There are three overlapping functions. The first is a stress recovery role. The second is to control energy balance through regulation of the intake, storage, and utilisation of food. The third involves immune regulation; endocannabinoid signalling is activated by tissue injury and modulates immune and inflammatory responses. Thus, the endocannabinoid neuromodulatory system appears to be involved in multiple physiological functions, such as anti-nociception, cognition and memory, endocrine function, nausea and vomiting, inflammation, and immune recognition		Somnolence or sedation, confusion, psychosis. The content of THC and CBD in medical cannabis is highly variable and ranges from 1% to 22% THC and 0.05% to 9% CBD. In contrast the THC/CBD concentration in THC/CBD (nabiximols) oromucosal spray and the THC content in plant-derived and synthetic THC are standardised	There is no high-quality evidence for the efficacy of any cannabis-based product including herbal cannabis (marijuana) in any condition with chronic neuropathic pain. Some adverse events (particularly somnolence or sedation, confusion, psychosis) may limit the clinical usefulness of cannabis-based medicines. It might be expected that, at best, a few people with neuropathic pain will benefit from long-term use of cannabis-based medicines.	

Topical treatments (e.g. Ibuprofen gel)	Topical salicylates are thought to relieve pain by irritating the skin. Topical non-steroidal anti-inflammatory's (NSAIDs) penetrate the skin and inhibit an enzyme involved in inflammation, reducing the sensitisation of the danger receptor. Capsaicin is derived from chillies is thought to desensitise danger receptors by over stimulating them, reducing their ability to signal danger. Lidocaine is a local anaesthetic which blocks danger receptors and messages.	There is some evidence that suggests that topical nsaids do help with knee and hand OA but in no other painful conditions. Using nsaids topically rather than orally reduces the risk of adverse side effects.	They all have the potential to produce side effects mainly of local skin irritation	There is evidence for topical diclofenac in OA, sprains and strains with low NNT. but no evidence for other chronic painful conditions. A recent review of high dose of capsaicin in 2017 showed moderate levels of pain relief though quality of the evidence was low. There is no evidence to support the use of topical salicylate, low dose capsaicin clonidine or lidocaine though the evidence does not exclude beneficial effects in a small percentage of people.	

Oral NSAIDs	NSAIDs act by inhibiting the cyclooxygenases (COXs), which synthesise prostaglandins that are involved in inflammation and cause peripheral sensitisation.		Serious side effects to the gastrointestinal system including ulcers, abdo pain and bleeding. Some cause increased risk of cardiovascular problems. Monitoring including U7Es, LFTs, and hearing tests. Reye's syndrome	There is insufficient evidence to support or refute the suggestion that oral NSAIDs have any efficacy in any chronic pain condition. The absence of any reliable evidence of oral NSAID efficacy is a challenge to their continued widespread use. In the absence of any supporting evidence they should probably not be recommended.	

Antidepressants	Some inhibit the reuptake of serotonin, noradrenaline, some also inhibit reuptake of norepinephrine. These neurotransmitters are thought to modulate the ascending and descending danger messenger nerves. It is thought that the mechanisms could be similar to those underlying its antidepressant effect, or another distinct mechanism of action as it is thought that they start working on pain at much lower doses	They are thought to work at much lower doses for pain than for antidepressants hopefully minimising side effects.	Side effects include · Nausea · Dizziness · Drowsiness · Dry mouth · constipation · Weight gain · Insomnia · Serotonin syndrome · Suicide related behaviours · Rise in BP/pulse	Cochrane found no evidence to support their use apart from - · Amitriptyline where there was no evidence from trials but clinicians had reported years of successful treatment in patients with chronic pain so Cochrane suggested it could be used. · Duloxetine has evidence for the treatment of pain in diabetic peripheral neuropathy and lower quality evidence for other chronic pain conditions. The evidence was provided by the manufacturer so the suggestion was that more was needed led by an independent investigator. · Mirtazepine - On balance, any potential benefits of mirtazapine in fibromyalgia were outweighed by its potential harms, though, a small minority of people with fibromyalgia might experience substantial symptom relief without clinically-relevant adverse events.	

Antiepileptic	Some Antiepileptic's are thought to work by affecting GABA sites – GABA is the main inhibitory neurotransmitter, some by stabilising the danger messenger nerves. Some are thought to block new danger receptor formation.		Side effects include · Sedation · Dependence, tolerance, behavioural disinhibition in patients with psychiatric conditions (clonazepam) · Haematological reactions (carbamazepine) · Birth defects · Vision abnormalities · Decreased libido · Worsen heart failure · Weight gain · DRESS – Drug reaction with eosinophilia and systemic symptoms Monitoring needed – eye tests, U&Es and weight	For most there is no evidence for. Benefits have not been shown to outweigh the drug's potentially serious side effects. Gabapentin- evidence is biased and over half of those treated will not get worthwhile pain relief. In 2016 a review showed insufficient evidence to support or refute the suggestion that gabapentin reduces pain in fibromyalgia. This was reiterated in a review in Jan 2017 – evidence was weak and low quality and my benefit a few people with the condition. There is some evidence that for 3-4/10 people with post herpetic neuralgia and peripheral diabetic neuropathy get good levels of pain relief taking 1800-3600mg compared with 1-2/10 with placebo. Carbamazepine - like amitriptyline has no evidence base but as clinicians perceive it to work NICE have recommended it. For trigeminal neuralgia. Topiramate and Sodium valproate - some evidence to be effective for migraine prophylaxis versus placebo but more evidence is needed to compare against other available drugs. Pregabalin- is also commonly prescribed and is thought to have high levels of benefit for a minority of patients with chronic pain (post herpetic neuralgia and diabetic neuropathy). Some will not benefit. Recent review jan 2019 no change to above findings.	

Muscle relaxant	Some reduce muscle spasm (divided into benzodiazepines like diazepam and non-benzodiazepines e.g. methocarbamol) and others prevent increased muscle tone, spasticity that interferes with therapy or function (e.g. Baclofen).	These drugs are used to treat anxiety and promote sleep short term. Some reduce muscle spasm and others prevent increased muscle tone.	They can produce adverse effects including · Tolerance and dependency is the concerning one · Fatigue · Nausea · Headaches · Blurred vision · Dry mouth · Sexual dysfunction · Dizziness · Constipation · Confusion	There is evidence to suggest they can help in the very short term but because of adverse effects the need to be used with great caution. Taking drugs that are going to make you drowsy, confused will affect your ability to stay active which is the most important treatment for Chronic pain.	
Antipsychotics	They have been a controversial adjuvant analgesic in the past. They were thought to have an effect on certain neurotransmitters which would give analgesic effect		Side effects include drowsiness	Sedation is the main use for this when treating chronic pain but this side effect is usually unwanted	

Dietary supplements Glucosamine and chondroitin	Cartilage is the rubbery substance that cushions bones. The chemicals glucosamine and chondroitin occurs naturally in the body and is the building block for cartilage		Side effects include skin rashes, rise in blood glucose levels, asthma.	No evidence that this supplement is effective	

Invasive procedures	Procedures that involve disrupting the danger messages travelling to the brain by using an injection in your back. This could have been in the form of an anaesthetic, opiate, steroid, chemical/thermal/laser ablation aimed at destroying a part of your nervous system. The injections can be given into different parts of the spine (the space between the vertebrae, around the nerve roots or into the disc) also into ligaments and muscle	Possible short term pain relief	Many side effects including · Headache · Dizziness · Transient local pain · Tingling · Numbness · Nausea and vomiting · Itching · Rare serious complications include cauda equine syndrome, septic arthritis, discitis, paraplegia, Para spinal abscesses. · Steroids can weaken bones, increasing risk of fractures.	For all of the procedures the Cochrane reviews found no good quality evidence to say they should be used to manage chronic pain	

Physiotherapy / exercise	Not only does exercise help with releasing your body's natural endorphins that can effectively block some danger signals and produce feelings of relaxation (reduces cortisol response to stress), it can also help you to lose weight, improve your flexibility and balance.	See previous column	Usually needs patient engagement and motivation to be most effective	Evidence to suggest improvement in muscle strength and conditioning and some reduction in pain. Cochrane review 2016 showed physical activity and exercise may improve pain severity as well as physical function and quality of life. 2017 review into Yoga showed some evidence in favour for back related function and pain. Graded motor imaging and mirror therapy may provide improvements in pain and function in people with CRPS type 1.	
Chiropractor and Osteopaths	Aims to improve joint range of movement			No evidence that supports or refutes that chiropractic interventions provide a clinically meaningful difference for pain or disability in people with low back pain when compared with other interventions.	

TENS	A TENS machine is thought to electrically stimulate inhibitory neurones in the spinal cord and peripheral nerves blocking danger signals	Inexpensive safe. Can be self administered. Readily available without prescription.	Not indicated for use with broken or infected skin. Needs to be used around a local area	Cochrane states that there is no evidence to support the use in the routine management of chronic LBP. Review in oct 2017 no evidence for it's use in fibromyalgia. Overview of Cochrane reviews in April 2019 – no change to the above.	
Muscle energy technique	Inhibit muscles by activating opposing muscle groups to help restore joint range and function	Movement based manual therapy so help improve joint range of movement	No evidence to suggest any effectiveness for chronic pain	No evidence	
Aquatic training and resistance training for fibromyalgia	Improve muscle strength and endurance through a progressive exercise program	Helps improve strength and conditioning of muscles and also improves cardiovascular fitness	Requires engagement and motivation from patients to be effective	Some evidence for its effectiveness	
Massage	Said to improve blood flow and reduce muscle tone through hands on treatment	Aims to improve muscle tone and help with swelling		Only some low level evidence for its effectiveness so cannot be recommended	
Lumbar supports	Said to help support the muscles of the lower back and add stability	Aims to support the muscles of the lower back	Can reduce strength/ activation in muscles around the lower back	No evidence to support its effectiveness	

Exercise	Progressive exercise program to improve muscle strength and endurance	Aims to improve cardiovascular fitness, increase strength and can aid with weight loss	Requires engagement and motivation from patients to be most effective. Few adverse effects.	Slightly effective at reducing pain and increasing function in chronic low back pain. Graded activity in sub-acute back pain improves absenteeism. Quality of evidence is low. May improve pain severity and physical function and consequent quality of life. Potentially beneficial.	
Low level laser treatment	Non-invasive light source treatment that generates a single wavelength of light, no heat/sound/vibration. Believed to affect the function of connective tissue cells (fibroblasts), accelerate tissue repair and act as an anti-inflammatory agent.		None	Insufficient data to recommend.	

Psychological treatments	Strategies that are thought to improve psychological and physical wellbeing, aiming to allow patients to take an active role in their treatment. They include **Biofeedback** – use of technology to give audio or visual feedback on physiological processes. **Mindfulness** - a way of looking at the world in a non-judgemental manner **Movement therapies** – use of physical movement to stimulate mental clarity such as yoga, tai chi. **Psychological therapies** – use of techniques to help people become aware of their own thoughts and behaviours **Relaxation strategies** – techniques to help calm the mind and relax the body e.g. breathing techniques	· Improves wellbeing and management of chronic pain.	Difficult to get the right treatment at the right time due to waiting lists and because these treatments are often offered only when orthodox treatments have failed.	Cochrane – there is some evidence for psychological therapies improving physical functioning pain and low mood. Cochrane – internet delivered psychological therapies – promising Oct 18 – In children - Psychological treatments delivered predominantly face-to-face might be effective for reducing pain outcomes for children and adolescents with headache or other chronic pain conditions post-treatment. However, there were no effects at follow-up. Psychological therapies were also beneficial for reducing disability in children with mixed chronic pain conditions at post-treatment and follow-up, and for children with headache at follow-up. We found no beneficial effect of therapies for improving depression or anxiety. The conclusions of this update replicate and add to those of a previous version of the review which found that psychological therapies were effective in reducing pain frequency/intensity for children with headache and mixed chronic pain conditions post-treatment.	

Botox	Temporarily numbs or weakens nerves and muscles that might contribute to pain.	none	Many side effects	Temporarily numbs or weakens nerves and muscles that might contribute to pain. No evidence for it.	
CAM – Complementary and alternative medicine	We are unsure how these treatments work. The difficulty we have is their acceptance in a conventional western medicine system. Evidence from the East hasn't been made available and there are no drug companies going to sponsor a trial when they don't stand to gain financially.	There is some evidence for these practices. The difficulty we have is their acceptance in a conventional western medicine system	No scientific evidence to suggest why these treatments work.	Individuals can benefit from alternative medicine and as there is little side effects and no evidence to suggest a negative effect it may be worth trying	
Herbal remedies	We know that peppermint reduces substance P which is a pain neurotransmitter. Cochrane mentions evidence for Cayenne and Lavender.		Little evidence for the effectiveness of these treatments	Some patients may find this type of treatment beneficial	

Acupuncture	Is a form of Chinese medicine and uses fine needles to stimulate peripheral nerves, local inhibition of nociceptive fibres by releasing adenosine. It is thought to work by reducing inflammation, stimulating the release of your body's own pain killers (endorphins) and calming your brain by deactivating the limbic areas. There are a number of different techniques including traditional manual acupuncture, electropuncture and non thermal lasers.		There can be some side effects but these are usually short lived and can vary from session to session – consult with your practitioner to see if this type of treatment is suitable for you	A Cochrane review in December 2017 shows the data is limited. Insufficient evidence to support/refute the use of acupuncture.	

Non invasive brain stimulation	Non-invasive brain stimulation techniques aim to induce an electrical stimulation of the brain in an attempt to reduce chronic pain by directly altering brain activity. They include repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES), transcranial direct current stimulation (tDCS), transcranial random noise stimulation (tRNS) and reduced impedance non-invasive cortical electrostimulation (RINCE).		Lack of effect. Risk of seizures.	There is a lack of high-quality evidence to support or refute the effectiveness of non-invasive brain stimulation techniques for chronic pain. Due to the small size of included studies and limitations in the way that many studies were conducted, future studies may have a substantial impact upon the estimates of effects presented.	

Finally, Cochrane basically conclude that a multidisciplinary approach is needed, conventional analgesics are usually not effective and only a minority of individuals achieve worthwhile pain relief. You may have come to a similar conclusion yourself with your experiences of the medical model. We highlight the drugs that show evidence of being effective.