Treatment	**Level of Evidence** **Effect Size**	**Accessibility and Use**
Weight Loss	Strongest evidence of effect Approximately 50% improvement in pain with over 10% weight loss (1–4)	Patient adherence- may rebound Dietician- expense Slow results without guaranteed benefit
Exercise- Strength	Lots of studies confirm benefit for pain and function, including in severe OA awaiting surgery (5–8) Moderate effect size. Thought that high-intensity more beneficial, but higher level of adverse events Higher intensity associated with greater effect on pain and function (9)	No known critical dose potency, average 10% improvement in pain and function Risk for injury if not supervised- expense. Requires gradual progression Decline in adherence associated with diminishing effects over time
Exercise- General	Recommended for all levels of severity(6) Modulation of pain, upregulate inhibitory interneurons Can be tailored to reduce impact and load, including hydrotherapy (10)	Careful prescription to avoid exacerbation Gym- controlled environment but expense Target the specific impairments identified
Education and self-help strategies	Putative effect for general education CBT and Pain Coping Skills Training (PCST) appear to significantly reduce pain and improve function A recent RCT showed promising benefits of Teleconferencing education vs internet education (11)	Critical intervention for setting expectations and improving adherence to effective self-help treatments (diet and exercise) CBT often embedded within physiotherapy programs
Paracetamol	Statisfically significant but no clinically significant benefit over placebo (12,13) Many industry funded RCTs at risk of bias (14)	Commonly used and recommended May not be as safe as previously thought, with observational studies reporting dose responsive GI, renal and CV adverse events. More likely to have abnormal LFTs, but uncertain clinical consequence.

Opiates	No benefit over placebo (15)	Significant risk of side effects, tolerance and dependence (dose dependent effects)
NSAIDs	Evidence of efficacy Minimal clinically important difference commonly met in studies (16,17)	Multiple well documented risks
Duloxetine	Evidence of efficacy in chronic pain and moderate-severe knee OA(18)	Side effects and withdrawal effects Stigma associated with anti-depressants in pain management
Strontium	Evidence of reduced OA progression with bone marrow lesions Minimal clinical effects.	Fairly safe medication Industry-funded trials to date
Topical Analgesia	60% achieve 50% improvement in pain (NSAID) (17) 80% of patients have pain reduction with capsaicin (19)	Simple to apply, relatively cheap Mild skin irritation is main side effect
Neutriceuticals Glucosamine and Chondroitin	Early studies showed small but statistically significant effect Glucosamine HCl shown to have no benefit (20) One study demonstrated radiological evidence of slowed chondral loss with reduced joint space narrowing after 2-3 years of use (21) Recent systematic review shows no effect of combination (22)	Expense is not prohibitive May be no significant benefit, and therefore a trial for 3 months is a reasonable option
ASU Avocado Soybean Unsaponafiables	Same effect when compared to GC(23,24)	May be no significant benefit, and therefore a trial for 3 months is a reasonable option
Fish Oil	Shown to be effective in Rheumatoid arthritis,(25) but recent study showed higher benefit from low dose (with canola oil) compared to high dose formulation (26)	May be no significant benefit, and therefore a trial for 3 months is a reasonable option
TENS	Recent study shows no more effective than exercise alone (27)	Relatively cheap and widely available Used in conjunction with exercises to allow increased pain threshold

Arthroscopy (lavage or partial meniscectomy)	No benefit over sham surgery, even for meniscal tears (degenerative) (28–34)	Easy to perform and obtain MBS rebate Very accessible Potential harms are significant
Corticosteroid Injection	Short-term alleviation of synovitis (35) Catabolic effects on cartilage- Randomised trials have shown reduced chondral thickness when compared to saline (36)	Easy to administer May be done with or without ultrasound guidance
Platelet Rich Plasma Injection	Mostly positive benefit in studies, but there is high risk of bias in most studies (37–43) Up to 12 months benefit Only one placebo (saline) controlled RCT	Takes time to spin blood No MBS rebate for consult or injection. Expense around $400
Viscosupplementation Hyaluronic Acid Injection	Up to 9 months benefit Evidence of statistically significant benefit for pain and function, but small effect size (may not be clinically significant as does not meet minimal clinically important difference) (44–49)	Expense of nearly $500 for injectate alone Need a prescription to obtain
Stem Cells	Some studies show promise with radiological and histological benefit (50,50) No high quality evidence of efficacy Small studies at high risk of bias (49–54) Issues with theoretical rationale- presumption of cell integration and differentiation without any scaffold	Very expensive Liposuction may be seen as a benefit
Orthotic devices Insoles	Medial OA- lateral wedge- uncertain Lateral OA- 1 high quality study supports use of medial insoles (57)	May be expensive, often require customisation
Knee Braces	Benefit has been demonstrated in RCTs and meta-analyses particularly for Varus knees with medial compartment OA, although small when compared to placebo braces (58,59)	Expensive and may be cumbersome Compliance as low as 50% Usually reserved for moderate/severe OA (persistent symptoms) May have most effect in most active
Mobility Aids	Contralateral sided use of walking stick shown to reduce pain and increase function (60)	Cheap and easily prescribed Stigma associated with visible disability

Pain blockade	Tanezumab- NGF inhibitor Evidence of significant pain benefit- up to 50% change in baseline pain with walking in moderate-severe OA knee (61)	In trials- adverse events with rapid acceleration of osteoarthritis found. Uncertain safety.
Endocrine	Calcitonin- binds to calcitonin receptors on osteoclasts and inhibits bone resorption, whilst increasing activity of osteoblasts (62) Found to be ineffective compared to placebo	Oral and Intra-articular formulations
Growth factors	FGF-18- Sprifermin- increases proteoglycan synthesis and cartilage matrix formation. Statistically significant, dose-dependent improvement in tibiotfemoral cartilage volume and reduction of JSN at 12 months (63,64)	In early trials
Growth factors	BMP-7 AKA osteogenic protein-1- tissue repair and inhibition of catabolic cytokines (63)	In pre-clinical trials
Growth factors	TGF-beta- downstream effects include inhibition of matrix degrading metalloproteinase activities, upregulation of pain molecules like NGF which may be a cause for pain (64,65) Chemotaxis of MSCs and subchondral progenitor cells (66) Stimulates chondrogenesis in animal studies	In pre-clinical trials

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