Low back pain

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Low back pain covers a spectrum of different types of pain (eg, nociceptive, neuropathic and nociplastic, or non-specific) that frequently overlap. The elements comprising the lumbar spine (eg, soft tissue, vertebrae, zygapophyseal and sacroiliac joints, intervertebral discs, and neurovascular structures) are prone to different stressors, and each of these, alone or in combination, can contribute to low back pain. Due to numerous factors related to low back pain, and the low specificity of imaging and diagnostic injections, diagnostic methods for this condition continue to be a subject of controversy. The biopsychosocial model posits low back pain to be a dynamic interaction between social, psychological, and biological factors that can both predispose to and result from injury, and should be considered when devising interdisciplinary treatment plans. Prevention of low back pain is recognised as a pivotal challenge in high-risk populations to help tackle high health-care costs related to therapy and rehabilitation. To a large extent, therapy depends on pain classification, and usually starts with self-care and pharmacotherapy in combination with non-pharmacological methods, such as physical therapies and psychological treatments in appropriate patients. For refractory low back pain, a wide range of non-surgical (eg, epidural steroid injections and spinal cord stimulation for neuropathic pain, and radiofrequency ablation and intra-articular steroid injections for mechanical pain) and surgical (eg, decompression for neuropathic pain, disc replacement, and fusion for mechanical causes) treatment options are available in carefully selected patients. Most treatment options address only single, solitary causes and given the complex nature of low back pain, a multimodal interdisciplinary approach is necessary. Although globally recognised as an important health and socioeconomic challenge with an expected increase in prevalence, low back pain continues to have tremendous potential for improvement in both diagnostic and therapeutic aspects. Future research on low back pain should focus on improving the accuracy and objectivity of diagnostic assessments, and devising treatment algorithms that consider unique biological, psychological, and social factors. High-quality comparative-effectiveness and randomised controlled trials with longer follow-up periods that aim to establish the efficacy and cost-effectiveness of low back pain management are warranted.

Introduction

Low back pain covers a spectrum of different types of pain, including nociceptive pain, neuropathic (radicular) pain that travels down the legs, and in some cases, nociplastic pain, which is caused by amplification of pain in the CNS, often falling under the umbrella of non-specific low back pain. Frequently, these pain subtypes overlap (eg, a patient with a herniated disc who has back pain can have radicular pain and diffuse symptoms outside pathoanatomical referral patterns).

The low back is anatomically defined as extending from the 12th rib to the iliac crest, and although low back pain often coexists and is conflated with buttock pain, the buttock region is anatomically distinct and comprises a region from the iliac crest to the gluteal folds. Most people have at least one episode of acute low back pain in their lifetime. This condition is usually self-limiting, but often becomes chronic.[1] Studies have found that more than 60% of individuals with mechanical low back pain will continue to have pain or frequent recurrences 1 year after onset.[2] For new-onset lumbar radiculopathy, between 15% and 40% of people will have chronic pain or frequent relapse.[3] Chronic low back pain is a consequence of complex interactions encompassing biological, psychological, and social factors.[4]

It is important to understand that pain is distinct from nociception, and includes not just A delta fiber and C fiber activation, but also context-dependent emotional, cognitive, and behavioural elements.[5] This distinction partly explains the poor correlation with pathology and symptoms,[6] and why interventions that have no effect on degenerative processes (eg, psychological therapies or acupuncture) can have profound effects on pain and quality of life, whereas interventions that address pathology (eg, surgery) often do not provide benefit. This notion was eloquently described by Melzack and Casey[7] in their landmark classification of pain into sensory–discriminative, affective–motivational, and cognitive–evaluative components. It forms the basis for a multimodal, precision medicine approach to low back pain, and is a foundation for the biopsychosocial model.[8]

Search strategy and selection criteria

We searched MEDLINE, Cochrane Library, and Google Scholar using the key words "back pain", "spine OR spinal pain", with the qualifiers "low OR lumbar", "radicular", "neuropathic", "neurogenic", "mechanical", "axial", "buttock", and "non-specific" in combination with the terms "epidemiology", "pathogenesis", "clinical presentation", "diagnosis", "imaging", "therapy", "trials", and "prevention" from January, 1991, to January, 2021, with no date or language restrictions. We prioritised systematic reviews and meta-analyses, and clinical trials that multiple authors judged relevant, but did not exclude any data sources including non-peer-reviewed literature in the public domain. We also included review articles to provide readers with more details and more references than this Seminar permits.

In this Seminar, we provide a brief overview on epidemiology, and the causes and risk factors that contribute to the pathogenesis of low back pain. We also describe the clinical presentation and diagnostic evaluation of low back pain and different therapeutic options.

Epidemiology

A study done in 195 countries assessing the incidence, prevalence, and years lived with disability for 354 medical conditions found low back pain to be the leading cause of worldwide productivity loss as measured in years, and the top cause of years lived with disability in 126 countries.[9] One systematic review of 165 studies from 54 countries estimated the point prevalence of low back pain to be 11·9% (SD 2) and 1 month prevalence to be 23·3% (SD 2·9), and to be most common in middle-aged to older women (ie, 40–80 years).[10] The authors also found the incidence of low back pain to be lower in low-income and middle-income economies than high-income economies.[10] In 2019, a systematic review of 13 studies from North America, northern Europe, and Israel reported the prevalence to range between 1·4% and 20·0%, and the annual incidence ranging between 0·024% and 7%, being highest in the USA.[11] A systematic review and meta-analysis of the prevalence of low back pain in low-income, lower-middle, and upper-middle-income countries in Africa showed a pooled lifetime prevalence of 47%.[12] The prevalence of low back pain increases with age, with rates of 1%–6% in children aged 7–10 years, 18% in adolescents,[13] and a peak prevalence ranging from 28% to 42% in people between 40 years and 69 years.[10]

Low back pain can be classified as mechanical, radicular (neuropathic), or primarily nociplastic in nature, with the distinctions affecting treatment decisions. In studies that sought to determine the breakdown of lumbar pain, the prevalence of neuropathic pain has ranged between 16% and 55% in patients with chronic low back pain, with one review reporting an aggregate prevalence of 36·6%.[14] Radicular pain is most commonly associated with herniated nucleus pulposus and spinal stenosis, further stratified by location as central, foraminal, or involving the lateral recesses. Infrequently, other conditions (eg, herpes zoster and metastatic cancer) can cause radicular pain. The prevalence of radicular pain due to a herniated disc varies between 2% and 4%, being more common in men and in individuals aged between 30 years and 50 years.[15] The presence of a herniated nucleus pulposus does not always result in pain, with one systematic review reporting prevalence rates in asymptomatic individuals ranging from 29% in 20 year olds to 43% in 80 year olds.[16] Most herniated discs will regress within 2 years. In one review, the authors found that spontaneous regression occurred in more than 90% of sequestered discs, 70% of herniated discs, and more than 40% of protruded discs.[17] In another study, 87% of patients reported a decrease in acute pain due to disc herniation at 3 months.[18]

By contrast, spinal stenosis is an anatomically progressive condition and a direct consequence of age-related degenerative processes. However, not everyone with narrowing of the spinal canal will have radicular pain. In one review, the range of spinal stenosis in asymptomatic individuals ranged from 0% to 56%, with a median of 11%.[19] The authors of the Framingham Study[20] found prevalence rates of 22·5% for relative (lumbar spinal canal diameter ≤12 mm) and 7·3% for absolute acquired lumbar spinal stenosis (diameter ≤10 mm).

Nociplastic pain is the newest category of pain, with the primary pathology being central sensitisation. When experienced in the low back, this pain is often referred to as non-specific low back pain, although this term is often misapplied to individuals whereby the cause is unknown or ambiguous. Nociplastic pain can also accompany mechanical and neuropathic pain.[21]

Socioeconomic burden

The economic burden of low back pain is estimated to be around £2·8 billion in the UK[22] and more than AU$4·8 billion in Australia[23] per year. In the USA, the annual expenditures for the management of patients with low back pain are estimated to exceed US$100 billion.[24] A retrospective analysis of nearly 2·5 million US patients with newly diagnosed low back or lower extremity pain between 2008 and 2015,[25] revealed that 98·8% of cohorts did not undergo surgery in the year following diagnosis. The non-surgical cohort accounted for 26·3% of the total annual costs ($498 million) compared with $265 million annually for the surgical cohort.[25] Approximately two-thirds of the economic costs from low back pain stem from indirect costs (eg, loss of productivity).[26] Mutubuki and colleagues[27] found that female sex, young age, multiple causes, poor quality of life, and high disability (ie, functional impairment) were predictive of high societal costs (eg, health care or diminished productivity) among patients with chronic low back pain.[27] Another study showed that expenditures from presenteeism (ie, being present at work with suboptimal performance) were higher than direct medical costs.[28] The nature of low back pain could also result in less quantifiable costs such as difficulties doing domestic chores, caregiving, engaging in recreational activities, struggles with relationships, depression, and anxiety.[29]

Pathogenesis

Multifactorial causes and risk factors contribute to pathogenesis of low back pain, and this section provides an overview.

Disc degeneration

In a systematic review, Battié and colleagues[30] found inconsistencies when defining the term degenerative disc disease and identifying painful discs, which creates confusion in the literature and divergent treatment

algorithms. The structures constituting the lumbar spine include muscles, fascia, ligaments, tendons, facet joints, neurovascular elements, vertebrae, and intervertebral discs, all of which are susceptible to biochemical, degenerative, and traumatic stressors (figure 1).[31] The discs, which are 70–80% aqueous, are composed of an outer annulus fibrosus and inner nucleus pulposus. Intervertebral discs absorb shock, preserve spinal movements, and distribute axial and torsional forces. During healing, neovascularisation occurs and minute sensory nerves can penetrate the disrupted annulus and nucleus pulposus, leading to mechanical and chemical sensitisation.[32] Although MRI is highly sensitive for detecting disc pathology, a systematic review found conflicting evidence that endplate signal changes were associated with low back pain and activity limitations.[33] Another systematic review found only a modest correlation between disc space narrowing and low back pain in 26 107 patients.[34] Similar to other sources of mechanical pain, discogenic pain can extend into the upper and occasionally lower legs in a non-dermatomal pattern.

Radicular pain

Low back pain that extends into the leg, usually below the knee (radicular pain), can result from mechanical nerve root compression and chemical irritation from various inflammatory mediators that leak out of degenerated discs. Unlike referred pain from joints, muscles, and discs, the pain typically radiates in a dermatomal distribution. Herniated nucleus pulposus is the most common cause of radicular pain, although after 60 years of age, spinal stenosis is the leading cause. Spinal stenosis is most common at the L4–L5 level and can result from facet joint and ligamentum flavum hypertrophy, congenitally short pedicles, and spondylolisthesis.[35] Spinal stenosis can cause chronic mechanical compression resulting in axonal injury or nerve root ischaemia. Of note, however, is that both herniated nucleus pulposus and spinal stenosis are radiological diagnoses, and that not all people with stenosis and herniations have pain.

From a radiological perspective, absolute central lumbar stenosis refers to anteroposterior spinal canal diameter smaller than 10 mm, whereas foraminal stenosis relates to a neuroforaminal diameter smaller than 3 mm.[36] A herniated disc is diagnosed when the nucleus pulposus extends beyond the normal confines of the annulus fibrosis, but involves less than 25% of the circumference. Spinal stenosis often coexists with other conditions (eg, hypertrophied facet joints causing foraminal narrowing) including herniated disc, with one study reporting a 23% co-prevalence rate.[37] Because most herniated discs are substantially degenerated and the causes of spinal stenosis can also cause axial pain, most, but not all, cases of lumbar radicular pain co-occur with back pain.[38]

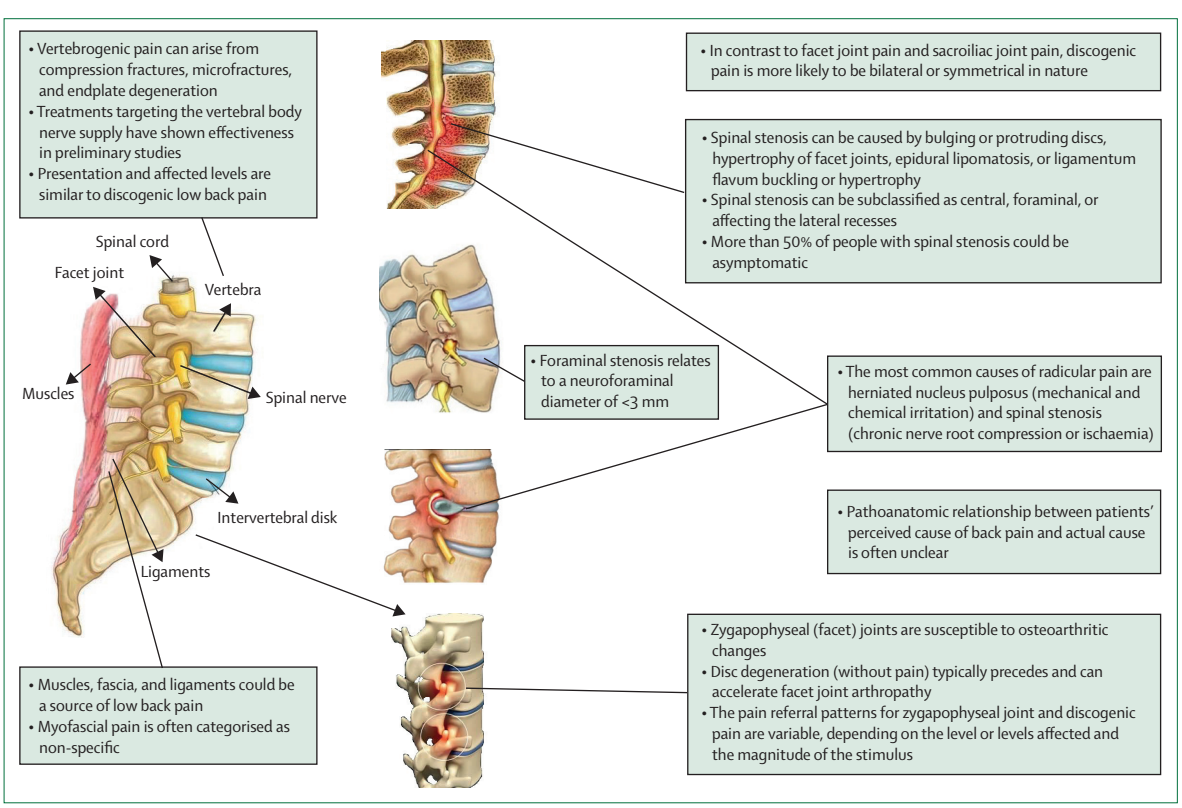

Figure 1: **Sagittal view of lumbar spine showing potential pain generators**

Facet arthropathy

Facet joints (ie, zygapophyseal joints) that connect adjacent vertebrae always play a role in limiting spine movements, but their role in loadbearing becomes prominent as discs age and degenerate. These joints are also prone to degenerative changes, most commonly osteoarthritis.[39] Referred lumbar facet joint pain has a variable presentation; upper lumbar levels are associated with non-dermatomal pain projecting into the hip, flank, and lateral aspects of the upper thigh, which is in contrast to pain felt in the lateral or posterior aspects of the thigh observed with the lower levels. The most commonly affected L4–L5 and L5–S1 zygapophyseal joints can sometimes produce pseudoradicular symptoms extending into the lower leg.[40]

Myofascial pain

Muscles, fascia, and ligaments can also be pain generators (figure 1).[41,42] Muscles that can potentially contribute to low back pain include deep intrinsic (eg, multifidus or rotatores) and the more superficial longissimus, spinalis, and iliocostalis muscles, collectively referred to as erector spinae muscles.[43] Back muscles are integral to normal spine stiffness and function, and chronic low back pain could be paradoxically associated with both atrophy and increased myoelectric activity, which is consistent with studies showing both increased and decreased activation depending on context.[43,44] Muscle pathology represents an underappreciated source of low back pain, often misdiagnosed as non-specific, and frequently arises consequent to other primary pathology. Myofascial pain might result from overuse, acute stretch injuries or tears, and diffuse or localised (eg, trigger points) muscle spasm.

Sacroiliac joint pain

The sacroiliac joint consists of an extensive network of ligaments both dorsally and ventrally, and a joint capsule in the anterior, lower-third of the sacroiliac junction. Although sacroiliac joint pain most frequently presents in the buttocks, over two-thirds of individuals will have lumbar pain; in approximately 50% of cases, the pain radiates to the leg, sometimes below the knee.[45] Both the ligaments and fibrous capsule are imbued with nociceptors and both could be a source of pain. Intra-articular pathology is more common in older people, whereas younger individuals with prominent tenderness and a traumatic cause are more likely to have extra-articular pathology.[46]

Spondyloarthropathies

Spondyloarthropathy refers to a family of inflammatory rheumatic diseases that includes ankylosing spondylitis and psoriatic arthritis. These systemic conditions typically include multiple joints, with ankylosing spondylitis and axial spondyloarthritis preferentially affecting the low back. In addition to facet and sacroiliac joint arthritis, other spinal manifestations include enthesitis and autofusion. The prevalence for spondyloarthropathies varies from 0·2%–0·5% for ankylosing spondylitis to 0·05%–0·25% for enteropathic axial arthritis.[47]

Nociplastic pain

The term non-specific low back pain is ambiguous and evolving. Semantically, the term refers to low back pain in which a specific pain generator, or generators, has not been identified—not that one does not exist. Historically, it has been written that approximately 90% of cases of low back pain were not associated with a clear-cut cause, although almost all studies used for this prevalence rate did not involve the use of advanced diagnostic tools (eg, diagnostic blocks or electrodiagnostic testing).[48] Many cases were attributed to myofascial pathology, which is present in a high proportion of patients, irrespective of whether there is a primary cause.[44] In the past 5 years, the term nociplastic pain has been introduced, in which objective abnormalities might or might not be present, but in which the principal mechanism is sensitisation of the nervous system. Just as neuropathic pain and nociceptive pain can co-exist, nociplastic pain can be present in cases of nociceptive or neuropathic low back pain.

Changes in the brain

Structural and functional changes in the brain have been generating interest as they might serve as biomarkers linking anatomical changes with pain. Studies have identified common and disease-specific changes in white and grey matter brain regions in patients with chronic low back pain, such as the dorsolateral prefrontal cortex thalamus, temporal lobes, and insula and primary somatosensory cortex, indicating that chronic pain is associated with structural reorganisation.[49] Functional changes, such as alterations in blood flow and metabolism, have also been described. A study on patients with low back pain has shown that deleterious anatomical and functional changes can be reversed with treatment.[50]

Behavioural factors

In line with the revised International Association for the Study of Pain[51] definition of pain, low back pain represents not just the sensory awareness of bodily harm, but also an emotional experience that can be influenced by other emotions (eg, fear, sadness, and anxiety). Psychologically traumatic events could precipitate or reinforce low back pain. In one study evaluating clinician-reported views on low back pain triggers (which could underestimate the incidence), 3·1% cited psychological factors as a primary determinant.[52]

In clinical studies, negative expectations have been shown to predict poor pain outcomes.[53] Patients' expectations are based on previous experience, cultural attitudes, health-care beliefs, context, and an understanding of their illness.[54]

Misinterpretations of pain as a sign of physical harm often lead to fear and avoidance behaviours that

further fuel disability, depression, and anxiety. Low back pain frequently leads fearful patients to avoid painful movements or activities, putting them in a vicious cycle of anxiety, avoidance, disability, and worsening pain.[55] A large meta-analysis on 15 623 patients with chronic musculoskeletal pain, including 6312 with chronic low back pain, found that higher levels of fear-of-pain, anxiety, and fear-avoidance beliefs were statistically significantly associated with pain and disability.[56]

Traditionally, low back pain was considered a result of injury. This model is not only overly simplistic but does not reflect the power of pain to instigate learning and adaptation. Individuals with low back pain learn to predict, control, and prevent painful events. Although these forms of learning are natural and adaptive in acute back pain situations, they can become detrimental in the long term and contribute to the persistence of pain and disability.

Learning to predict pain occurs by detecting non-nociceptive cues or events that precede or coincide with the occurrence of pain. The mechanism of such Pavlovian learning is that after such co-occurrences, the non-nociceptive event elicits an anticipatory fear response. Such associations not only incite pain-related fear, they also can lead to hyperalgesia.[57] Erroneous beliefs about the relationship between particular movements and pain are prevalent in patients with low back pain,[58] but are also found among health professionals.[59] For example, the use of expressions implying harm (eg, "Your spine looks like that of a 70-year-old") could inadvertently evoke pain-related fear. Similar to Pavlovian learning is the acquisition of harm expectations, which have shown to be potent predictors of recovery from back pain.[60]

A particular form of learning to control pain is avoidance learning; individuals with low back pain learn that when they avoid the predictive cues, the anticipated pain increase or injury is circumvented. The fear-avoidance model combines the cognitive, emotional, motivational, and behavioural aspects of pain-related behaviour into an integrated theoretical framework.[60] Whereas avoidance might be adaptive in the short term, its excessive or unnecessary deployment can have detrimental consequences in the long term.[61]

***Panel:* Risk factors associated with progression of acute to chronic low back pain**

- Genetic factors
- Female sex
- Lifestyle (eg, sedentary lifestyle, obesity, and smoking)
- Psychosocial factors (poor social support, anxiety, depression, and catastrophising)
- Poor coping mechanisms (eg, fear-avoidance behaviour)
- Traumatic injuries
- Occupational hazards (eg, construction work and other types of manual labour, poor job satisfaction, and hostile work environment)
- Secondary gain
- Greater disease burden (eg, higher baseline pain, greater disability, and opioid use)

Genetic factors

The genetic determinants of low back pain have received increased attention in the past decade and could someday be part of precision medicine algorithms. Carvalho-E-Silva and colleagues[62] found that heritability contributed 26% to lifetime prevalence of low back pain, 36% for functional limitations, and 25% to pain intensity in 1598 twins. A systematic review of 27 studies involving twins showed that the effects of heritability accounted between 21% and 67% of back pain burden.[63] One question raised by genetic studies is how individually identified genes contribute to low back pain (eg, through pain perception, accelerated spondylosis, predisposing psychopathology, lifestyle, and response to treatments), and the role that epigenetics plays. Risk factors related to acute to chronic low back pain progression are listed in the panel.

Clinical presentation

Intervertebral disc herniation typically manifests as low back pain (ie, from annular tears and disc disruption) and leg pain (from nerve root irritation or referred pain from degenerated discs). This pain usually resolves over several weeks in patients without neurological deficits but might persist in many people. A prospective cohort study followed 605 patients with low back pain with or without sciatica for 2 years, and noted that 54% of patients had recurrent pain at 6 months and 47% had recurrent pain at 24 months.[64] The extent of disc herniation does not correlate well with severity of pain.[65] Patients with lumbar spinal stenosis can report low back and leg pain, aggravated by walking and alleviated by bending forward. They often present with a wide-based gait and neurological weakness.[35] These symptoms are referred to as intermittent neurogenic claudication,[66] which can be distinguished from vascular claudication in that patients with the latter could have decreased temperature in their feet, diminished distal pulses, and a lower ankle–brachial index. Patients with lumbar spinal stenosis can often be distinguished from patients with a herniated lumbar disc in that they tend to assume a characteristic kyphotic standing posture (flexion of the lumbar spine) to alleviate their symptoms, and physical examination signs, such as the straight leg raising test, are less reliable.[35] Clinical presentation and diagnostic evaluation of low back pain are shown in table 1.

Diagnosis of low back pain

An overview of 15 clinical practice guidelines explored diagnostic recommendations for non-specific low back pain.[74] Although a large proportion of low back pain cases

	Risk factors	Onset of condition	Clinical presentation*	Physical findings†	Diagnostic imaging
Mechanical pain					
Intervertebral disc[34,67,68]	Advanced age, but patients typically younger than those with facetogenic or sacroiliac joint pain; repetitive or acute trauma	Insidious	Low back pain and leg pain; pain worse with sitting	Midline tenderness; reduced range of motion, especially bending forward; no focal neurological findings	Plain films to evaluate disc height; MRI to detect annular tears, fissures, or high intensity zones; imaging not routinely needed
Facet joint[69]	Osteoarthritis; spondylolisthesis	Insidious	Axial low back pain; referred pain to hip, flank, or upper thigh	Paraspinal greater than midline tenderness; reduced back range of motion; no focal neurological findings	CT is gold standard for bone pathology, with SPECT scans showing correlation with facet block results; imaging not routinely needed
Muscles, fascia, and ligaments[68]	Strenuous activity; repetitive or abrupt movements (eg, coughing, sneezing)	Acute or insidious	Axial low back pain; occasional referred pain to the posterior thigh	Muscle guarding, spasm, oedema, or atrophy; reduced back range of motion; no focal neurological findings	Ultrasound; imaging not routinely needed
Sacroiliac joint[67,69]	Bimodal age distribution; trauma; pregnancy; previous surgery; spondyloarthropathy; advanced age; leg length discrepancy	Often follows trauma in the form of axial loading and abrupt rotation	Buttock pain; low back pain frequently radiating into the leg or groin; sitting or rising from sitting can worsen it	Tenderness near posterior superior iliac spine; pain worse with rising from sitting; no focal neurological findings	X-rays and radionuclide bone scans have low sensitivity; CT most sensitive for bone involvement; MRI might detect active inflammation and soft tissue pathology
Vertebral body	Advanced age, history of trauma	Insidious	Low back pain, with or without upper leg pain	Midline tenderness, pain worsened by activities, no focal neurological findings	Plain films to evaluate for acute compression fracture, MRI to detect endplate signal changes and acuity (eg, active inflammation)
Radicular pain					
Herniated disc[37,68,70]	Peak frequency age 30–50 years, more frequent in men with heavy lifting; trauma; lifestyle habits (smoking, obesity); symptoms can be caused by inflammatory cytokine release from discs	Acute or insidious	Low back pain or leg pain, or both	Straight leg raising test; crossed straight leg raising test; dermatomal pain location; diminished reflexes depending on nerve root involvement; lower extremity muscle weakness depending on nerve root involvement; weakness can be pain-induced or neurological	MRI for nerve root compromise (sensitivity 0·25; specificity 0·92); CT or CT myelography to differentiate soft tissue changes from osteophytes; imaging recommended for serious or progressive neurological deficits
Spinal stenosis[71–73]	Advanced age, hypertrophy of facet joints and ligamentum flavum; degenerative spondylolisthesis; disc bulging; congenital (eg, short pedicles)	Insidious	Low back pain and leg pain; wide-based gait; neurological weakness	At least three to five findings from patient history and examination (age >48 years, leg pain greater than back pain, bilateral symptoms, pain with walking or standing, pain alleviation with sitting); improved walking ability with the spine flexed forward; pain relief with bending; muscle weakness and diminished reflexes depending on nerve root involvement	MRI for soft tissues and measuring spinal canal diameter; CT can assess osseous diameter of spinal canal in axial views, but is less sensitive than MRI; plain x-rays used to evaluate spinal instability (flexion or extension)

SPECT=single photon emission tomography. *There is considerable overlap within radicular causes (eg, spinal stenosis and herniated disc) and within mechanical causes (eg, sacroiliac joint pain, facet joint pain, and degenerative discs), with frequent co-occurrence. †Historical and physical findings tend to be more sensitive than specific, and are not pathognomonic.

Table 1: **Clinical presentation and diagnostic evaluation of low back pain**

are non-specific or resolve without a formal diagnosis, most guidelines recommend history taking and physical examination to identify specific entities. Most guidelines (78%) endorsed neurological examination to identify patients with nerve root compression. Patients with lumbar spinal stenosis might also require vascular-focused studies to differentiate between vascular and neurogenic claudication.[35] More than half of the guidelines favoured triaging patients into three categories: non-specific low back pain, specific mechanical low back pain, or radicular pain; the remainder were against separate classification. The recommendations were uniform against the endorsement of imaging in patients with non-specific low back pain; however, more than half of the guidelines recommended imaging in patients with so-called red flags, with most also endorsing the assessment of so-called yellow flags during evaluation, which can lead to interventions that can prevent persistent disability (figure 2).

A large retrospective review showed that presence of red flags such as fracture, metastases, and infection increased the probability of identifying serious spinal pathology, although a negative response to red flag surveillance did not lower the probability of a red flag diagnosis.[76] A comprehensive analysis of 21 guidelines for the management of low back pain found inconsistencies as to which red flags to use for the detection of serious spinal pathology.[73] Other flags associated with prognosis for low back pain include orange (psychiatric symptoms), yellow (beliefs, appraisals, judgements, emotional responses, and pain-related behaviour), blue (relationship between work

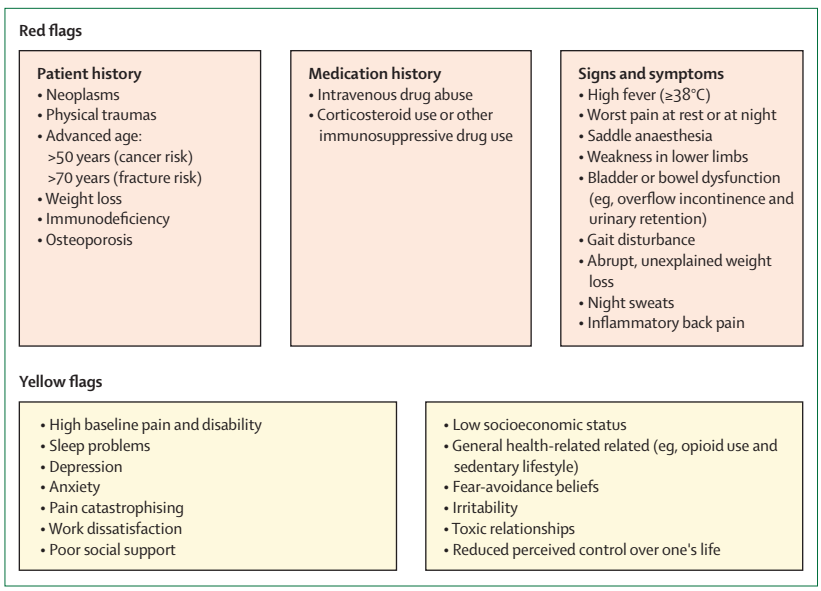

Figure 2: **Red and yellow flags for low back pain**[73,75]

and health), and black (system or contextual obstacles) flags.[76,77]

Imaging

Numerous guidelines have been published on the use of imaging for low back pain, high rates of use, the high prevalence rates of abnormalities in asymptomatic volunteers (most people have disc degeneration by age 40 years), and the poor correlation between symptoms and pathology.[78] For acute low back pain, red flags, including severe or progressive neurological deficits, warrant imaging. For chronic low back pain, routine imaging is not recommended, although it could be considered on a case-by-case basis, particularly when findings are likely to affect care (eg, referral for surgery).[79,80] Plain films can be considered when evaluating for spinal instability (flexion and extension), spondylolisthesis, or screening for scoliosis. MRI has not been shown to improve outcomes for patients who are candidates for epidural steroid injection,[81] but can contribute to higher rates of spine surgery and result in higher satisfaction rates.[82] In patients who are candidates for MRI but have contraindications, CT scans have greater than 90% sensitivity for detecting most lumbar pathology.[83]

Screening

Screening tools have been developed to identify patients with acute low back pain who are prone to develop chronic pain. The Örebro Musculoskeletal Pain Screening Questionnaire,[84] which assesses 24 different variables, was found to have low-to-moderate positive predictive values. The StarT Back tool[85] was developed to identify subgroups of patients with low back pain requiring early prevention strategies. A large prospective study found the StarT Back tool to be acceptable for a 1 year disability prediction, but it did not show discriminative value for future pain.[86]

Several instruments have been developed to distinguish neuropathic pain from non-neuropathic pain, including painDETECT, s-DN4, and s-LANSS.[87] These questionnaires have shown strong correlation, and can be self-administered, although physician designation is the reference standard. Questionnaires used to identify nociplastic contributions to low back pain can include the central sensitisation inventory and pain sensitivity questionnaire.[88]

Prevention

Prevention of low back pain has received increased attention as governments and payers struggle to find practical solutions to implement. One reason behind the lack of progress could be the underestimation of non-anatomical aspects contributing to low back pain, such as psychosocial risk factors,[89] and under-utilisation of multidimensional interventions.[90] Previous studies on interventions such as exercise, education, and ergonomic modifications have yielded modest results.[91] In adults, a systematic review found moderate-quality evidence that exercise alone or with education was effective for both primary and secondary prevention of low back pain, and low-quality evidence that education alone, back braces, shoe inserts, and ergonomic corrections were ineffective for the primary prevention of low back pain.[92] A systematic review confirmed that exercise alone and in combination with education was effective as a primary prevention strategy for low back pain.[93]

Treatment

Behavioural management of low back pain

Due to ongoing concerns about the risk to benefit ratio of opioids and suboptimal results in clinical trials evaluating other pharmacological agents, published guidelines have proposed non-pharmacological approaches such as exercise and physical therapy as first-line treatments for low back pain. The initial encounter with patients with low back pain should take place in a primary care setting,[31] and begin with familiarising an individual with their pain condition and self-management techniques. Should reassurance and self-care not work, additional risk-stratified methods such as exercises and cognitive behavioural therapy can be considered. If low back pain persists, pharmacological and procedural options can be trialed.

The management of chronic low back pain is notoriously challenging, and the prominent role of negative expectations, pain-related fear, and various avoidance behaviours in sustaining chronic low back pain,[94] warrant a behavioural management approach.[95] Yet, there is also no consensus as to what constitutes an optimal design or duration of treatment.[96] A range of psychological treatments for individuals with chronic pain has emerged in the past five decades, and those

sharing the goal of restoring the pursuit of individual-valued life goals can be roughly classified into clarification-oriented and exposure-based cognitive behavioural interventions. Clarification-oriented interventions help patients disengage from disabling avoidance behaviours by unambiguously providing new information that pain can be self-managed and does not require aggressive protection.[97]

Exposure-based treatments include graded activity, which uses operant learning principles to encourage healthy behaviours,[98] and exposure treatment, which focuses on the reduction of pain-related fears and maladaptive avoidance behaviours.[99] In a systematic review evaluating cognitive behavioural therapy for subacute back pain, most included studies reported statistically significant benefit at variable follow-up periods.[100] Cognitive behavioural therapy has also been shown to decrease recovery time and prevent the development of chronic spinal pain.[101] Future research in the area of behavioural treatments should aim to customise interventions. A systematic review on mindful-based stress reduction found only small, short-term differences for improvement in pain and function.[102] A systematic review of acceptance and commitment therapy on chronic low back pain revealed small to medium effect sizes for measures of function, anxiety, and depression, but not for pain or quality of life.[103]

Non-pharmacological treatment options

Oliveira and colleagues[74] summarised recommendations from 15 clinical practice guidelines for the management of non-specific low back pain. 11 of 12 guidelines recommended against bed rest for acute low back pain, and four were against bed rest for any duration of pain. More than half endorsed maintaining normal activities as part of acute low back pain management. Employing a multidisciplinary rehabilitation team was endorsed by nine of 11 guidelines for chronic low back pain. The American College of Physicians published guidelines with recommendations for non-invasive management of radicular or non-radicular low back pain.[104] The different types of non-pharmacological integrative treatments are shown in table 2.

Pharmacological treatment options

Pharmacological treatments might be ideal for patients with multiple areas of pain and multiple low back pain contributors, for individuals who are procedure-averse or at high risk for complications, and for individuals with nociplastic pain. According to the American College of Physicians guidelines,[104] pharmacological recommendations for acute or subacute low back pain should begin with non-steroidal anti-inflammatory drugs (NSAIDs) or muscle relaxants (moderate-quality evidence). There is no consensus on the duration of NSAID use, and caution is advised with persistent use due to concerns for gastrointestinal and cardiovascular adverse events. A Cochrane review found no significant difference on effectiveness between selective and non-selective NSAIDs for low back pain.[111] Guidelines by the American College of Physicians[104] recommend tramadol or duloxetine as second-line treatment, and opioids as the last-line treatment for chronic low back pain. The National Institute for Health and Care Excellence (NICE) guidelines[112] recommend not routinely using opioids for acute low back pain, and against their use for chronic low back pain.[113] Although opioids are as or more efficacious than other analgesics for both neuropathic and non-neuropathic pain,[114] a meta-analysis showed only modest, short-term pain relief in patients with chronic low back pain.[115] The addictive potential of opioids coupled with a plethora of side-effects have led multiple organisations to recommend them only for low back pain refractory to other treatments.[104]

Gabapentinoids are recommended by most organisations for the treatment of neuropathic pain;[114] however, a systematic review found no strong evidence to support their use for chronic low back pain with or without radicular pain.[116] Tricyclic antidepressants are also used in the management of neuropathic pain, and the serotonin–norepinephrine reuptake inhibitor duloxetine is approved by the US Food and Drug Administration for musculoskeletal pain, including low back pain. A systematic review by Chou and colleagues[117] found evidence supporting duloxetine, but not tricyclic antidepressants and gabapentinoids for chronic low back pain. However, the evidence for duloxetine in lumbosacral radiculopathy was indeterminate.

Non-surgical procedures

There is wide geographical and practitioner variability in the use of procedures to treat low back pain, and studies have shown positive correlations between imaging, injections, and surgery rates.[118] Given the risks and finite duration of benefit for interventions, procedures should generally be done on patients who have not responded to conservative measures, although exceptions could be reasonable in some cases.

Lumbar epidural steroid injections and adhesiolysis

Despite over 9 000 000 epidural steroid injections performed each year in the USA, the utility of lumbar epidural steroid injections is controversial, with studies and reviews done by interventionalists more likely to yield positive findings than those done by non-interventionalists.[119] For example, although the Spinal Intervention Society guidelines[120] give strong evidence to support lumbar epidural steroid injections for radicular pain, a Cochrane review found only small, short-term benefits compared with placebo for pain relief and function.[121] For axial low back pain, there is a shortage of strong evidence supporting benefit, and most guidelines recommend them only for radicular pain.

	Description	Effects
Massage[105]	Manual therapy to reduce muscle spasm and increase joint mobility	Immediate benefit for non-specific low back pain *vs* no treatment, inactive controls, or sham treatments, although differences in improvements are small; most beneficial as an addition to exercise or education
Acupuncture[105]	Manual needle insertion into particular points of different anatomical planes to reduce pain	Global improvement compared with NSAIDs but the effect is very small; inconsistent benefit for pain relief compared with NSAIDs; acupuncture in addition to medication is more effective for pain relief and function versus medication alone—differences are small; immediate pain relief and functional improvement greater than with sham acupuncture, no treatment, NSAIDs, or muscle relaxants—differences are small; systematic reviews have also found that some forms of sham acupuncture are superior to no treatment
Superficial heat and cold[106]	Increases cutaneous blood flow and causes a cooling reaction; can be done with moist hot packs, fluid therapy, whirlpool, or paraffin; used to relieve muscle spasms, joint contractures, and decreased range of motion	Short-term (4 days) pain and disability reduction for continuous heat wrap *vs* oral placebo in acute and subacute low back pain (≤3 months); additional benefit as an add-on therapy to exercise; insufficient evidence for chronic low back pain; insufficient evidence on the effects of cold therapy
Psychological therapies (CBT and operant therapy)[105]	CBT involves managing pain by modifying maladaptive beliefs and behaviours through education and methods to manage symptoms; operant therapy involves learning through positive reinforcement of health-promoting behaviours	Compared with waiting list control group or no psychological therapy, operant therapy and CBT show superior short-term post-treatment pain improvement; no therapeutic difference at 6 months
Yoga[105]	Ancient Indian practice whereby physical, mental, and spiritual exercises are used to improve bodily posture, and emotional and physical well-being	Yoga is superior to non-yoga exercise for pain and function in chronic low back pain (>12 weeks) patients; better function in the short term (≤3 months) and long term (≤1 year)
Tai chi[105]	Ancient Chinese art practiced as a graceful series of slow and focused movements accompanied by deep breathing	Tai chi as stand-alone or add-on therapy can improve pain and function
Movement control exercise[107]	Physical exercises designed to straighten muscles, alleviate pain, and improve spinal posture	Positive effect of movement control exercise on disability immediately after treatment and after 12 months
SMT[105]	Chiropractic application of controlled manipulation or thrust applied to joints of the spine	SMT is better than sham SMT and inert interventions and as an adjunct to other interventions for pain and quality of life improvement; non-significant short-term (1–3 months) effect on pain or function versus sham manipulation. Improvement in functional status as adjunct to other interventions
TSET[108]	Simultaneous application of electronic technological systems with exercise therapy	Technological support of physical exercises provides limited benefit for pain, disability, and quality of life; TSET is not more effective than other treatments
Mini-interventions[109,110]	Interventions based on features from light mobilisation and graded activity programmes	Mini-interventions reduce daily subacute low back pain symptoms, improve adaptation to pain, and do not increase health-care costs

CBT=cognitive behavioural therapy. NSAIDs=non-steroidal anti-inflammatory drugs. SMT=spinal manipulative therapy. TSET=technology-supported exercise therapy.

Table 2: **Non-pharmacological integrative treatments for low back pain**

There are several approaches for the administration of epidural steroids including transforaminal, interlaminar, and caudal routes. A comprehensive review of published data found strong evidence for transforaminal epidural steroid injection in herniated nucleus pulposus for up to 6 months, but only low-quality evidence for a small effect for spinal stenosis.[122]

For the type of steroid, all placebo-controlled trials have been done using long-acting particulate steroids, but reviews are mixed regarding whether they provide better or longer relief than non-particulate steroids (eg, dexamethasone).[122,123] However, the transforaminal delivery of long-acting particulate steroids has been associated with rare, catastrophic events such as death and paralysis, which has prompted some,[123] but not all,[124] task forces to recommend that the initial transforaminal lumbar epidural steroid injection be done with non-particulate steroids. Stratified by pathology, the effectiveness of epidural steroid injection tends to be better in patients with herniated nucleus pulposus than spinal stenosis, and weakest in individuals with axial pain and radicular pain from degenerative disc disease without nerve compression.[119] Most of the early (<2 weeks) effects of epidural steroid injection derives from the injectate itself (ie, local anesthetic and saline) rather than the steroids, which prompts questions about what constitutes a placebo for epidural steroid injection.[125,126] Although multiple studies have found evidence for long-term benefit with serial lumbar epidural steroid injections,[127,128] the disadvantage is that a single injection typically provides only short-term relief (<3 months). For the prevention of surgery, a meta-analysis found mixed evidence for a small effect in the short term for a single lumbar epidural steroid injection, but not in the long-term (>1 year).[129]

Sacroiliac joint injections

Small controlled studies with short-term (≤2 months) follow-up found evidence for intra-articular and extra-articular steroids in patients with and without spondyloarthropathy.[130] There is some evidence that the combination of intra-articular and extra-articular sacroiliac joint steroid injections might have a better therapeutic effect.[131] Fluoroscopic guidance has been recommended when doing sacroiliac injections; however, there is no agreement on the type and dose of steroids used.[131]

Facet joint blocks and radiofrequency ablation

Facet joints receive innervation from medial branches of the dorsal ramus at two levels, which are the target for diagnostic or prognostic nerve blocks. International guidelines on lumbar facet interventions found no evidence for long-term therapeutic benefit from medial branch blocks or intra-articular injections with steroids, and concluded that medial branch blocks should be the preferred prognostic test before radiofrequency ablation.[132] However, another evidence-based guideline provided moderate strength of recommendations for both lumbar facet joint nerve blocks and lumbar radiofrequency ablation.[133]

A large randomised controlled trial (RCT)[134] raised questions about the efficacy of radiofrequency treatment of the medial branches of the dorsal ramus; however, the study was widely criticised for its non-rigorous selection criteria and performance.[135,136] According to NICE guidelines,[112] radiofrequency lumbar medial branch (facet) denervation might be considered after conventional management has not worked in individuals with injection-confirmed facetogenic pain.

Sacroiliac joint radiofrequency

The sacroiliac joint is innervated by the lateral branches stemming from L5 to S3, and sometimes S4 dorsal rami. At each level, 1–4 lateral branches supply nociceptive feedback, primarily from the ligaments; hence, sacroiliac joint denervation is ideally suited for individuals with suspected extra-articular pain. Although there are numerous uncontrolled trials that have reported benefit, randomised placebo-controlled trials evaluating sacroiliac joint denervation are divided by efficacy, with most of the positive studies both being industry funded and using internally cooled electrodes.[137]

Spinal cord stimulation

A systematic review that compared spinal cord stimulation with conventional therapies in more than 300 000 patients with chronic low back pain and leg pain found that eight of 11 studies reported spinal cord stimulation to be associated with better outcomes and cost-effectiveness.[138] A review found low-to-moderate quality evidence that spinal cord stimulation is better than reoperation or conventional medical management for failed back surgery syndrome, but conflicting evidence that conventional spinal cord stimulation is superior to sham stimulation.[139] Major limitations of randomised spinal cord stimulator trials include the effect of industry sponsorship, including programming by company representatives, and the complete absence of adequate blinding.[139]

Spinal cord stimulation has traditionally been used for neuropathic pain, particularly in individuals with previous spine surgery and more pain in their legs than their backs. However, a study showed that high-frequency spinal cord stimulation provided better analgesia and functional improvement than conventional spinal cord stimulation in patients with low back and leg pain, with or without previous surgery.[140] A meta-analysis showed that neuromodulation was associated with opioid reduction.[141] Other major advances in neuromodulation include burst stimulation, MRI-compatible systems, dorsal root ganglion stimulation, and a diverse combination of electrode arrays.

Surgery

There has been enormous interest in the past two decades about the indications and utility of surgery for chronic low back pain. Studies have shown that surgical rates and the proportion of complex surgeries (eg, instrumentation) are higher in the USA than nearly all other countries, but do not affect low back pain disability rates.[142]

For herniated nucleus pulposus, a systematic review found that surgery results in faster pain relief and functional improvement than conservative management, but no differences were observed after 1–2 years.[143] In 2020, an RCT found greater improvement in the surgical group compared with conservative care in patients with sciatica secondary to herniated nucleus puplosus that persisted at 12 months.[144] In patients with lumbar spinal stenosis, a systematic review found that decompression surgery resulted in substantial improvement compared with conservative management at 3–6 months; at the 2–4 year follow-up, pain and disability outcomes continued to be more favourable in the surgical group, but had declined.[145] A later systematic review found no benefit for decompression and fusion compared with decompression alone for stenosis.[146] The 2016 NICE guidelines[112] recommend spinal decompression for people with radicular pain when non-surgical treatment has not improved pain or function, and radiological findings are consistent with radicular symptoms.

Lumbar fusion is often done for refractory spondylosis. However, a meta-analysis that included studies with long-term follow-up found little benefit for fusion compared with non-operative management.[147] A cohort study evaluating prognostic factors following fusion found that older patients (62 years old *vs* 57 years old) undergoing single-level lumbar disc fusion with low baseline disability had the best outcomes.[148] According to the NICE guidelines,[112] spinal fusion should not be offered as a treatment for low back pain outside of a clinical trial.[112]

Patients with low back pain who undergo spinal surgery could have recurrent low back pain with or without a radicular component, termed as failed back surgery syndrome. The incidence ranges from 10% to upwards of 40% after lumbar laminectomy, with or without fusion.[149] Causes might include adhesions, arachnoiditis, spinal instability, complications of the surgery (battered nerve roots), inappropriate patient selection, technical failure, and adjacent segment disease.

Disc replacement is generally limited to individuals with predominantly discogenic pain at one or two segments,

and might be associated with better preserved range of motion than arthrodesis. A systematic review that compared lumbar fusion with disc replacement reported short-term benefits favouring disc replacement that might not have been clinically meaningful.[150] An earlier Cochrane review reported disc replacement to have small, clinically questionable benefits compared with fusion surgery and comprehensive rehabilitation in patients with degenerative disc disease.[151] An inherent flaw in surgical studies that use intention-to-treat analysis is that more patients crossover to the surgery group than vice versa, which can minimise differences.[144]

Limitations

Conclusions from narrative reviews rely heavily on article selection, and although we prioritised systematic reviews and meta-analyses, the conclusions in these reviews vary with specialty, which introduces bias. Unlike conditions such as diabetic neuropathy, low back pain is a symptom; therefore, studies evaluating interventional treatments tailored towards a specific cause (eg, injections or surgeries) depend on accurate diagnosis, which is subject to false-positive and false-negative results. Non-pharmacological treatments (integrative and procedural) are challenging to study using placebos (eg, ethical and practical [enrollment] concerns about invasive sham treatments, ambiguity about what constitutes a placebo), and uncontrolled studies generally overestimate treatment effects. There are also numerous therapies that we were not able to evaluate in this Seminar, and the decision about which ones to include were based on what we considered important.

Major challenges for this Seminar were the multifactorial nature of most cases of chronic low back pain (eg, superimposed facetogenic pain, discogenic pain, and muscle tension), and the inherent difficulties in identifying pain generators (eg, low MRI specificity, and the high false-positive and false-negative rate of diagnostic blocks with no reliable reference standards); the high placebo response rate for surgery, non-surgical interventions, and integrative therapies that require multiple visits and hands-on care; deciding what constitutes a true control (eg, placebo) treatment, and the cost and ethics involved in doing controlled studies; and poor translation from clinical trials to clinical practice.

Future directions for low back pain research include the shift from focusing on outcome measures based on self-report only (eg, pain scores at a cross-section in time) to behavioural and neurocognitive measures (eg, step count and functional imaging); increasing the duration of follow-up in clinical studies; avoiding unnecessary provider contact; taking steps to maximise study blinding effectiveness; adapting study designs that consider personalised care models; including patients with psychopathology, on opioid therapy, and with a nociplastic component to enhance generalisability; and determining the relationship between infection and disc degeneration, and the effectiveness of antibiotics to treat disc disease.

Conclusions

The prevalence of chronic low back pain is expected to increase with the ageing of populations and as technological advances lead to more sedentary lifestyles. Although this Seminar focuses on specific conditions and their treatments, there is considerable overlap between contributors to low back pain in terms of presentation. There is widespread acceptance of the biopsychosocial model that emphasises multidimensional components and the diverse consequences of chronic pain that can adversely affect all aspects of life. This model emphasises behavioural and lifestyle modification and the burgeoning fields of genetics and phenotyping (ie, precision medicine), a detailed discussion of which is beyond the scope of this Seminar. Although most currently available pain management options typically address only single causes, given the complex nature of low back pain, a multimodal, interdisciplinary approach is warranted.

Contributors

NNK and SPC conceived the design, and NNK, JWSV, and SPC searched the published work. All authors contributed to the writing of the Seminar and approved the submitted version.

Declaration of interests

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