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What is low back pain and why we need to pay attention

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Summary

Low back pain is a very common symptom. It occurs in high-, middle-, and low-income countries and all age groups from children to the elderly. Globally, years lived with disability caused by low back pain increased by 54% between 1990 and 2015, primarily due to population increase and ageing, with the biggest increase seen in low- and middle-income countries. It is now the leading cause of disability worldwide. For the vast majority of people with low back pain, it is not possible to accurately identify the specific nociceptive source and only a small proportion have a well-understood pathological cause, for example, a vertebral fracture, malignancy or infection. People with physically demanding jobs, physical and mental comorbidities, smokers and obese individuals are at greater risk of reporting low back pain. Disabling low back pain is overrepresented among people with lower socioeconomic status. Most people with new episodes of low back pain recover quickly; however, recurrence is common and in a small proportion of people low back pain becomes persistent and disabling. Initial high pain intensity, psychological distress and accompanying pain at multiple body sites increases the risk of persistent disabling low back pain. There is increasing evidence that central pain-modulating mechanisms and pain cognitions play important roles in the development of persistent disabling low back pain. Cost, health care utilization, and disability from low back pain vary substantially among countries and are influenced by local culture and social systems, as well as beliefs about cause and effect. Disability and costs attributed to low back pain are projected to increase in coming decades in particular in low- and middle-income countries, where health and other systems are often fragile and not equipped to cope with this growing burden. Intensified research efforts and global initiatives are clearly needed to address the burden of low back pain as a public health problem.

Key points

- Low back pain is an extremely common symptom in populations around the world and occurs in all age groups from children to the elderly
- Low back pain was responsible for 60.1 million disability-adjusted life years in 2015, an increase of 54% since 1990, with the biggest increase seen in low- and middle-income countries
- Disability from low back pain is highest in working age groups worldwide, which is particularly concerning in low- and middle-income countries where informal employment is common and possibilities for job modification are limited
- Most episodes of low back pain are short-lasting with little or no consequence, but recurrent episodes are common and low back pain is increasingly understood as a long-lasting condition with a variable course rather than episodes of unrelated occurrences
- Low back pain is a complex condition with multiple contributors to both the pain and associated disability, including psychological factors, social factors, biophysical factors, comorbidities, and pain-processing mechanisms
- For the vast majority of people with low back pain it is currently not possible to accurately identify the specific nociceptive source
- Lifestyle factors such as smoking, obesity, and low levels of physical activity that relate to poorer general health are also associated with occurrence of low back pain episodes
- Costs associated with health care and work disability attributed to low back pain vary considerably among countries, and are influenced by social norms, health-care approaches, and legislation
- The global burden of low back pain is projected to increase even further in coming decades, particularly in low- and middle-income countries

Introduction

Low back pain is an extremely common symptom and experienced by people of all ages.¹⁻³

In 2015, the global point prevalence of activity-limiting low back was 7.3%, implying that 540 million people were affected at any one point in time. Low back pain is now also the number one cause of disability globally.⁴ The largest apparent increases in disability caused by low back pain in recent decades occurred in low- and middle-income countries including Asia, Africa, and the Middle East⁵, where health and social systems are poorly equipped to deal with this growing burden in addition to other priorities such as infectious diseases.

Rarely can a specific cause of low back pain be identified; thus, most low back pain is termed non-specific. It is well-accepted that low back pain is characterised by a range of biophysical, psychological, and social dimensions that impair function, societal participation, and personal financial prosperity. The financial impact of low back pain is cross-sectoral as it increases costs in both healthcare and social supports systems.⁶ Disability attributed to low back pain varies considerably among countries, and is influenced by social norms, local health care approaches, and legislation.⁷ In low and middle income countries formal and informal social-support systems are negatively affected. Whilst in high income countries the concern is that the prevalent health care approaches for low back pain contribute to the overall burden and cost rather than reducing it.⁸ Spreading high-cost health-care models to low- and middle-income countries will compound rather than alleviate the burden. Low back pain is therefore an urgent global public health concern.

Against this backdrop, we present a series of three papers. The aim of this paper is to present a current understanding of what low back pain is, its burden and global impact as

well as an overview of causes and the course of low back pain. The evidence for the effectiveness of currently used treatments and promising new directions for managing low back pain is presented in paper two,⁹ and paper three is a worldwide call to action.¹⁰

The approach for this series involved the constitution of a team of leading international experts on back pain from different professional backgrounds and from countries around the globe who convened for a workshop in Buxton, UK in June 2016 to outline the structure of each paper. For this paper, we have identified scientific studies using broad search terms in MEDLINE (PubMed) and Scopus. To identify potentially relevant papers from low- and middle-income countries, we have also searched Google Scholar and the African Index Medicus Database. In an attempt to minimize selection bias and to ensure high-quality evidence was selected, systematic reviews were preferred and sought where possible. However, we also used information from large population-based cohorts, international clinical guidelines, and the Global Burden of Disease 2015 study. Primary research from low- and middle-income regions excluded from systematic reviews was also referenced where appropriate.

What is low back pain?

Low back pain is a symptom not a disease, and can result from several different known or unknown pathologies or diseases. It is defined by the location of pain, typically between the lower rib margins and the buttock creases.¹¹ Low back pain is commonly accompanied by pain in one or both legs and some people with low back pain have associated neurological symptoms in the lower extremities.

For the vast majority of people presenting with low back pain, it is not possible to identify the specific nociceptive source and those affected are then classified as having ‘non-specific’ low back pain.¹² There are some serious causes of low back pain (malignancy, vertebral fracture, infection or inflammatory disorders such as axial spondyloarthritis) that require identification and specific management targeting the pathology, but these account for a small proportion of cases. People with low back pain often experience concurrent pain in other body sites, as well as more general physical and mental health problems, compared to people not reporting low back pain.¹³ The combined effect on individuals of low back pain and comorbidity is often more than the effect of the low back pain or the comorbidity alone and results in more care, yet typically a poorer response to a range of treatments.¹³ Thus, many people living with low back pain have diverse problems in which psychological, social, and biophysical factors as well as comorbidities and pain processing mechanisms impact on both the pain experience and the associated disability (Figure 1).

Potential nociceptive sources of non-specific low back pain

Although clinical tests are unable to accurately identify the tissue source of most low back pain, several structures are innervated and have been shown to produce pain when stimulated. In some cases local anaesthetic relieves the pain (Table1).^{14,15}

Many imaging (X-ray, CT Scan and MRI) findings identified in people with low back pain are also common in people without low back pain, and their importance in diagnosis is a matter of substantial debate.¹⁶ Nevertheless, at least in people aged <50 years, some MRI abnormalities are more common in people with low back pain than in those without. A

systematic review (14 case-control studies; 3097 participants) found several MRI findings had a reasonably strong association with low back pain including Modic type 1 change (OR 4.0 [95% CI 1.1–14.6]), disc bulge (OR 7.5 [1.3–44.6]), disc extrusion (OR 4.4 [2.0–9.7]) and spondylolysis (OR 5.1 [1.7–15.5]) (Table 2).¹⁷ However, there is insufficient evidence to know whether MRI findings predict the future onset, or the course, of low back pain.¹⁸ Importantly, there is no evidence that imaging improves patient outcomes¹⁹ and guidelines consistently recommend against the routine use of imaging for people with low back pain.²⁰⁻

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Neurological symptoms associated with low back pain

Radicular pain and radiculopathy

Radicular pain occurs when there is nerve-root involvement; this is commonly termed sciatica. The term sciatica is used inconsistently, by clinicians and patients for different types of leg/back pain and should be avoided.²⁴ The diagnosis of radicular pain relies on clinical findings including a history of dermatomal leg pain, leg pain worse than back pain, worsening of leg pain during coughing, sneezing or straining²⁵ and straight leg raise test. Radiculopathy is characterised by the presence of weakness, loss of sensation, and or loss of reflexes associated with a particular nerve root, and can co-exist with radicular pain. People with low back pain and radicular pain or radiculopathy are reported to be more severely affected and have poorer outcomes as compared to patients with low back pain only.²⁶ Disc herniation in conjunction with local inflammation is the most common cause of radicular pain and radiculopathy. Disc herniation is, however, a frequent finding on imaging in the asymptomatic population,¹⁶ and disc herniations often resolve or disappear over time independent of resolution of pain.²⁷

Central lumbar spinal stenosis

Lumbar spinal stenosis is clinically characterised by pain or other discomfort with walking or prolonged standing that radiates into one or both lower extremities and is typically relieved by rest or lumbar flexion (neurogenic claudication).²⁸ It is typically caused by narrowing of the spinal canal or foramina due to a combination of degenerative changes such as facet osteoarthritis, ligamentum flavum hypertrophy, and bulging discs. There is expert consensus that the diagnosis of the clinical syndrome of lumbar spinal stenosis requires both the presence of characteristic symptoms and signs as well as imaging confirmation of narrowing of the lumbar spinal canal or foramina.²⁹ Symptoms of central lumbar spinal stenosis are thought to result from the venous congestion or ischemia of the nerve roots in the cauda equina due to compression.²⁸

Specific pathological causes of low back pain

Potential causes of low back pain that may require specific treatment include vertebral fractures, inflammatory disorders such as axial spondyloarthritis, malignancy, infections, and intra-abdominal causes (Table 3). A study of 1,172 new presentations of acute (< two weeks) episodes of low back pain in primary care in Australia found specific causes of back pain in 0.9% of participants, with fracture being by far the most common (8/11), followed by inflammatory disorders (2/11).³⁰ A Ugandan review of 204 patients referred to a hospital orthopaedic clinic with a primary complaint of low back pain showed that 4% had serious spinal pathology due to tuberculosis, 3.5% had vertebral compression fractures, 1% brucellosis, and 1% had malignancy.³¹ These differences in the patterns of specific pathological causes may reflect the ongoing burden of infectious diseases and their

manifestations as low back pain in low income countries. 'Red flags' are case history or clinical findings believed to increase the risk of a serious pathology, however, 80% of people with acute low back pain have at least one 'red flag' despite <1% having a serious disorder.³⁰ Nearly all recommended individual 'red flags' are uninformative and do not substantially change post-test probabilities of a serious pathology.³² The very low specificity of most red flags contributes to unnecessary specialist referrals and imaging.³³ Clinicians do, however, need to consider if the overall clinical picture might indicate a serious cause for the pain, remembering that the picture can develop over time.³³ The US guideline for imaging advises deferral of imaging pending a trial of therapy when there are weaker risk factors for cancer or axial spondyloarthritis.³⁴

How common is low back pain?

Low back pain is uncommon in the first decade of life, but prevalence increases steeply during the teenage years; around 40% of 9-18-year olds in both high-, medium-, and low-income countries report having experienced low back pain.^{35,36} Most adults will experience low back pain at some point.³⁷ The median one-year period prevalence globally in the adult population is around 37%, it peaks in mid-life and is more common in females (Figure 2).¹ Low back pain that is accompanied by activity limitation increases with age.³⁸ The mean prevalence in high-income countries is higher than in middle- and low-income countries (32.9% (SD 19.0) vs 25.4% (SD 25.4) vs 16.7% (SD 16.7)), but globally there is no difference between rural and urban areas.¹ Jackson pooled results from 40 publications dealing with prevalence of persistent low back pain in 28 countries from Africa, Asia, the Middle East, and South America (n = 80,076) and found that chronic low back pain was 2.5 (95% CI 1.21-

4·10) times more prevalent among workers relative to non-working populations for reasons that are not clear.³⁹ The gender pattern in low- and middle-income regions may also differ from that of high-income countries and even differ among low-income regions. For example, males seem to report low back pain more often than females in Africa.³⁶ This was not the case in Latin America,⁴⁰ which may reflect African culture where males often perform hard physical labour as well as gender inequalities, which may result in women underreporting their low back pain.

Burden and impact of Low Back Pain

Overall disability

The Global Burden of Disease (GBD) 2015 study calculated disease burden for 315 causes in 195 countries and territories from 1990 to 2015 and provides a comprehensive assessment of the patterns and levels of acute and chronic diseases and burden and disability of those across the globe.⁴¹ Low back pain was responsible for around 60·1 million years lived with disability (YLD) in 2015, an increase of 54% since 1990.⁴ It is the number one cause of disability globally, as well as in 14 of the 21 GBD world regions.⁴ Less than 28% of prevalent cases (n = 151 million) fell in the severe and most severe categories, however these accounted for 77% of all disability caused by low back pain (46·5 million YLDs).⁴² Thus, the majority of people experiencing low back pain have low levels of disability but the additive effect of those, combined with high disability in a substantial minority, result in the very high societal burden. **In high-income countries, disabling back pain is linked to socioeconomic status, job satisfaction, and the potential for monetary compensation (Table 4).**⁴³ The overall increase in the global burden of low back pain is almost entirely due to

population increase and ageing in both high-income and low- and middle-income countries, as opposed to increased prevalence.^{1,44}

Work disability

Disability from low back pain is highest in working age groups worldwide (Figure 3),^{4,41} which is particularly concerning in low- and middle-income countries where informal employment is common and possibilities for job modification are almost completely absent. Furthermore, occupational musculoskeletal health policies such as regulations for heavy physical work and lifting are often absent or poorly monitored.⁴⁵ A survey of 10,839 residents of an urban black community in Zimbabwe found that low back pain was among the top five reported primary health complaints, and reasons for activity limitation⁴⁶. A survey among 500 farmers in rural Nigeria revealed that over half reduced their farming workload because of low back pain.⁴⁷ Thus disability associated with low back pain may contribute to the cycle of poverty in poorer regions of the world.

In high-income countries, differences in social compensation systems, not differences in occupational exposure or individual factors, are largely responsible for national differences in the rates and extent of work disability attributed to low back pain.⁷ In Europe low back pain is the most common cause of medically certified sick leave and early retirement.⁴⁸ However work disability due to low back pain varies considerably among European countries. For example, in Norway and Sweden in 2000 short-term sickness absence rates in people with back pain were similar (5.1% & 6.4% respectively), but the rate of longer-term medically certified sickness absence was very different (22% and 15% respectively).⁴⁹ In the

US, low back pain accounts for more lost workdays than any other occupational musculoskeletal condition,⁵⁰ but while 58 out of 10,000 US workers filed a back-related claim in 1999, the comparable figure from Japan during the same year was only 1 out of 10,000.⁵¹

Social identity and inequality

The impact of low back pain on social identity and inequality is substantial all over the world. Ethnographic interviews of villagers in Botswana revealed that low back pain and other musculoskeletal symptoms resulted in both economic and subsistence consequences as well as loss of independence and social identity because of inability to fulfil traditional and expected social roles in a society with harsh living conditions.⁵²

Froud, reviewing 42 qualitative studies all from high income countries, found that many people living with low back pain struggled to meet their social expectations and obligations and that achieving these might then threaten the credibility of their suffering, with disability claims being threatened. Although those with back pain seek to achieve pre-morbid levels of health, many find with time that this is unrealistic and live with reduced expectations.⁵³

Likewise MacNeela reviewed 38 separate qualitative studies also from high income countries and found that worry and fear about the social consequences of chronic low back pain, hopelessness, family strain, social withdrawal, loss of job and lack of money, disappointment with health care encounters (in particular with general practitioners), coming to terms with the pain, and learning self-management strategies were common themes.⁵⁴

Globally, low back pain contributes to inequality. In low- and middle-income countries, poverty and inequality may increase as participation in work is affected. Further, formal return-to-work systems are often not in place, and workers may be retrenched, placing more strain on family and community livelihoods.⁴⁵ In Australia, Schofield demonstrated that individuals who exit the workforce early as a result of their low back pain, have substantially less wealth by the age of 65 years, even after adjusting for education.⁵⁵ The median value of accumulated wealth for those who retire early due to low back pain is only \$5,038 by the time they reach 65 years of age, compared to \$339,121 for those who remain in the workforce.⁵⁵

Cost of low back pain

No relevant studies on costs associated with low back pain from low- and middle-income countries were found. Costs associated with low back pain are generally reported as direct medical (health care) costs, and indirect (work absenteeism/productivity loss) costs. Only a few studies have reported on other direct nonmedical costs such as costs from transportation to appointments, visits to complementary and alternative practitioners, and informal help not captured by the health care system, which means that most studies underestimate the total costs of low back pain (Table S1). The economic impact related to low back pain is comparable to other prevalent, high-cost conditions such as cardiovascular disease, cancer, mental health and autoimmune diseases.⁶ Replacement wages account for 80-90% of total costs, and consistently a relatively small percentage of cases account for these.⁵⁶ Some of the observed variation in costs for low back pain over time may be explained by changes in disability legislation and health care practices. For example, in the

Netherlands costs associated with low back pain were substantially reduced between 1991 and 2007 following a change in legislation that reduced disability pensions and applied evidence-based criteria for medical practices.^{7,57}

Estimates of direct medical costs associated with low back pain are also all from high-income countries, with the US having the highest costs due to a more medically intensive approach and higher rates of surgery compared to other high-income countries (Table S2).^{8,58} In the UK in 2006, one in seven of all recorded consultations with general practitioners were for musculoskeletal problems with complaints of back pain being the most common (417 consultations per year for low back pain per 10,000 registered persons),⁵⁹ and in South Africa low back pain is the sixth most common complaint seen in primary health care.⁶⁰ In addition to conventional medicine, complementary and alternative medical approaches are popular with people who have low back pain. In the US for example, 44% of the population used at least one complementary or alternative health care therapy in 1997;⁶¹ and the most common reason was low back pain.⁶²

Natural history of low back pain

Low back pain is increasingly understood as a long-lasting condition with a variable course rather than episodes of unrelated occurrences.⁶³ Around half of the people seen with low back pain in primary care have a trajectory of ongoing or fluctuating low- to moderate-intensity pain, some recover, and some have persistent severe low back pain.⁶⁴ A systematic review (33 cohorts; 11,166 participants) provides strong evidence that most episodes of low back pain improve substantially within six weeks and by 12 months average pain levels are low (6 points on a 100-point scale; 95% CI 3–10).⁶⁵ However, two thirds of patients still

report some pain at three months; 67% (95% CI 50–83%) and 12 months; 65% (95% CI 54–75%).^{65,66} Recurrences of low back pain are common but a 2017 systematic review (7 studies; 1,780 participants) found the available research does not provide robust estimates of the risk of LBP recurrence. The best available evidence suggests around 33% of people will have a recurrence within one year of recovering from a previous episode.⁶⁷

Risk factors and triggers for episodes of LBP

While the impact of low back pain in low- and middle-income countries on systems and people differ from high-income countries, there appear to be fewer fundamental differences in the aetiological pathways among regions. A systematic review (eight cohorts; 5,165 participants) found consistent evidence that people who have had previous episodes of low back pain are at increased risk of a new episode.⁶⁸ Likewise, people with other chronic conditions including asthma, headache and diabetes are more likely to report low back pain than people in good health (pooled ORs 1.6 to 4.2).⁶⁹ People with poor mental health are also at increased risk. For example, a UK cohort study (5,781 participants) found psychological distress at age 23 predicted incident low back pain ten years later (OR 2.52 [95% CI 1.65–3.86]).⁷⁰ The Canadian National Population Health Survey with 9,909 participants found that pain-free individuals with depression were more likely to develop low back pain within two years when compared to people without depression (OR 2.9 [95% CI 1.2–7.0]).⁷¹ Mechanisms behind the co-existence of low back pain and other chronic diseases are not known but systematic reviews of cohort studies indicate that lifestyle factors such as smoking,⁷² obesity,^{73,74} and low levels of physical activity,⁷⁵ that relate to poorer general health are also associated with occurrence of low back pain episodes or

development of persistent low back pain, although independent associations remain uncertain.

A systematic review (seven twin studies; 35,547 participants) found the genetic influence on the liability to develop low back pain ranged from 21% to 67% with the genetic component being higher for more chronic and disabling low back pain than for inconsequential low back pain.⁶⁹ A comprehensive genetic epidemiologic analysis including 15,328 Danish twins (44% monozygotic and 56% dizygotic) found that heritability estimates for pain in different spinal regions were quite similar and there is a moderate to high genetic correlation between the phenotypes, which may indicate a common genetic basis for a high proportion of spinal pain.⁷⁶

An Australian case-crossover study (999 participants) found that awkward postures (OR 8.0 [95% CI 5.5–11.8]), heavy manual tasks (OR 5.0 [95% CI 3.3–7.4]), feeling tired (OR 3.7 [95% CI 2.2–6.3]) or being distracted during an activity (OR 25.0 [95% CI 3.4–184.5]) were all associated with incidence of an episode of low back pain.⁷⁷ Similarly, work exposures of lifting, bending, awkward postures and tasks considered physically demanding were also associated with an increased risk of developing low back pain, which is also the case in low- and middle income countries.^{36,40} A systematic review (25 cohorts) found that the effect of heavy workload on onset of low back pain ranged from OR 1.61 (95% CI 1.08–2.39) to OR 4.1 (2.7–6.4).⁷⁸ The existence of a causal pathway between these risk factors and low back pain, however, remains unclear.⁷⁹

We found no data on risk factors and triggers for episodes of low back pain from low- and middle-income countries. It is unclear if risk factors in low- and middle income are substantially different from high-income countries.

Multifactorial contributors to persistent disabling low back pain

Over recent decades the biopsychosocial model has been applied as a framework for understanding the complexity of low back pain in preference to a purely biomedical approach. Many factors including biophysical, psychological, social and genetic factors, and comorbidities (Figure 1) can contribute to disabling low back pain (Table 4). However, there are not firm boundaries among these and they all interact with each other. Thus, it is clear that persistent disabling low back pain is not simply a result of nociceptive input. While there are substantially fewer data from low- and middle-income countries the available data suggest similar multifactorial contributors seem to be important as in high income countries.⁸⁰

Biophysical factors

While the role of biophysical impairments in the development of disabling low back pain is not fully understood, impairments are demonstrable in people with persistent low back pain. One example is that some people with persistent low back pain may have alterations in muscle size,⁸¹ composition,⁸² and coordination⁸³ that differ from those without pain. These changes may be more than merely a consequence of pain and are only partly influenced by psychological factors.⁸⁴

Psychological factors

Psychological factors are often investigated separately, but there is a substantial overlap of constructs such as depression, anxiety, catastrophizing, and self-efficacy. The presence of these factors in people who present with low back pain is associated with increased risk of developing disability even though the mechanisms are not fully understood (Table 4). For

example, in a UK cohort study including 531 participants, pain-related distress explained 15% and 28% of the variance in pain and disability respectively.⁸⁵ The fear-avoidance model of chronic pain (including low back pain), which describes how fear of pain leads to the avoidance of activities and thus to disability, is well established. This has more recently been expanded to capture the influence of maladaptive learning processes and disabling beliefs on pain perception and on behaviours, suggesting that pain cognitions play a central role in the development and maintenance of disability, and more so than the pain itself.⁸⁶ A systematic review including 12 mediation studies identified self-efficacy, psychological distress, and fear as intermediate factors explaining some of the pathway between experiencing neck or back pain and developing disability.⁸⁷ The potential importance of self-efficacy is supported by a systematic review (83 studies; 15,616 participants) of chronic pain conditions (23 low back pain studies) that found self-efficacy to be consistently associated with impairment and disability, affective distress and pain severity.⁸⁸ Therefore some chronic pain treatments have shifted away from aiming to directly alleviate pain to aiming at changing beliefs and behaviours.⁸⁹

Social and societal factors

Chronic disabling low back pain affects people with low income and short education disproportionately. In a UK study of 2,533 people, life-time socio-economic status predicted disability due to any pain condition in older age (independent of comorbid conditions, psychological indicators and BMI) (OR 2.04 [95% CI 1.55–2.68]).⁹⁰ Cross-sectional data from the USA (National Health Interview Survey 2009-2010, 5,103 people) found that those with persistent low back pain were more likely to have had less than high school education (OR 2.27 [95% CI 1.53–3.38]) and had annual household income < \$20,000 (OR 2.29 [1.46–

3-58).⁹¹ Suggested mechanisms for the effect of low education on back pain include environmental and lifestyle exposures in lower socio-economic groups, lower health literacy, and health care not being available or adequately targeted to people with low education.⁹² Also, being in routine and manual occupations, **having less satisfying work, or having higher physical workloads is associated with disabling low back pain after one year (Table 4).**⁴³

Central pain processing/modulation

Nociceptive input is processed throughout the nervous system including modulation within the spinal cord and supra-spinal centers. In chronic pain, supra-spinal centers can show varying levels of activation and can be recruited for activation (or not) in a dynamic fashion contingent on nociceptive drive, context, cognition and emotion. If any of these factors change, the same nociceptive input can produce a different cerebral signature in the same subject.⁹³ A systematic review (27 studies; 1,037 participants) found moderate evidence that chronic low back pain patients show structural brain differences in specific cortical and subcortical areas, and altered functional connectivity in pain-related areas following painful stimulation.⁹⁴ The clinical implication of these findings remains to be clarified.⁹³

Multivariable Predictive models

Pain intensity, psychological distress, and accompanying pain in the leg or at multiple body sites are identified as predictors across externally validated multivariable predictive models developed to identify people at particular risk of developing disabling low back pain, (Table S3). In a systematic review (50 studies; 33,089 participants) the average amount of variance

explained in seven development samples was 43%, indicating that most of the variation between individuals is due to unknown or unmeasured factors.⁹⁵

Limitations

Despite advances in many aspects of understanding low back pain including the burden, course, risk factors, and causes, some important limitations exist. The vast majority of existing evidence comes from high-income countries, and may or may not generalise to low- and middle-income countries. While many factors are associated with both the development of low back pain and the transition to persistent disabling pain, the underlying mechanisms, including the influence of co-occurring non-communicable diseases, are poorly understood. Despite the burden of low back pain, research is often not considered a priority in low- and middle income countries, and thus the consequences of low back pain in these settings are largely unknown. The functional domains used in GBD 2015 do not take into account broader aspects of life such as participation, wellbeing, social identity, carer burden, use of healthcare resources, and work disability costs. In cost studies, a top down approach is most often used and those may not capture all costs as seen from the individual point of view in specific contexts.

Conclusion

Low back pain is now the number one cause of disability globally. The burden from low back pain is increasing particularly in low- and middle-income countries, and this is straining health care and social systems that are already overburdened. Low back pain is most

prevalent and burdensome in working populations, and in older people low back pain is associated with greater activity limitation. Most cases of low back pain are short-lasting and a specific nociceptive source cannot be identified. Recurrences are, however, common and a small minority of cases end up with persistent disabling pain influenced by a range of biophysical, psychological, and social factors. Costs associated with health care and work disability attributed to low back pain are enormous but vary considerably among countries, and are influenced by social norms, health care approaches, and legislation. While there are several global initiatives to address the global burden of low back pain as a public health problem, there is a need for further research to identify cost-effective and context-specific strategies for managing LBP in order to mitigate the consequences of the current and projected future burden.

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Contributors

JH and MU was part of team that developed the original proposal for the series and coordinated production of papers. JH and MH led the drafting of this paper in collaboration with the other authors. AK, QL, and MU closely revised many sections. Thereafter all authors have contributed to all sections of the paper and have edited it for key intellectual content. JH, MH, AK, JK, MF, SG, RS, QL, GP and MU participated in the authors' meeting, drafted different sections of the paper and took part in discussions during the drafting process. All other authors have read and provided substantive intellectual comments to the draft and approved the final version of the paper.

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Declarations of Interest

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Table 1: Potential nociceptive contributors to low back pain that have undergone investigation

Potential nociceptive contributor	Description
Intervertebral disc	While some imaging and clinical findings increase the likelihood that pain is arising from the intervertebral disc (using the reference standard of discography), there is no investigation that is able to accurately identify a disc problem as contributing to an individual's pain. ¹⁴ There is no widely accepted reference standard for discogenic pain.
Facet joint	Injecting facet joints with local anaesthetic can cause temporary relief of pain. ¹⁵ However the Framingham Heart Study (3,529 participants) found no relationship between radiological osteoarthritis of facet joints and presence of low back pain. ⁹⁶ It is not possible to identify clinically those individuals whose facet joints are contributing to their pain. ⁹⁷
Vertebral Endplates (Modic changes)	Modic changes are vertebral endplate abnormalities seen on MRI with specific subchondral and vertebral bone marrow features that can be classified according to different signal intensities into type 1, type 2 and type 3. Endplate defects and disc herniation may predispose to the development of Modic changes. One theory is that the pro-inflammatory response, caused by structural damage to the disc or endplate, may allow microbial infiltration and/or autoimmune reactions that intensify and prolong nociceptor stimulation by chemical or mechanical stimuli. ⁹⁸ A low-grade infection by <i>Propionibacterium acnes</i> may promote the development of Modic changes. ⁹⁹ The relevance of these finding to clinical practice is, however, unclear. A systematic review concluded that Modic type 1 changes are associated with low back pain (Table 2). ¹⁷ A subsequent study including 1,142 people found that Modic type 2 changes were associated with disability (OR 1.56 [95% CI 1.06–2.31], but not pain (OR 1.36 [0.88–2.09]). ¹⁰⁰ It is not possible to identify individuals in whom Modic changes are contributing to their pain.

Table 2: Strength of association between MRI findings and LBP in younger adults. Modified from Brinjikji et al 2015¹⁷

Imaging finding	No. of studies	OR (95% CI)	Prevalence asymptomatic (95% CI)	Prevalence symptomatic (95% CI)	P-value	Heterogeneity
<i>Intervertebral disc degeneration related outcomes</i>						
Disc degeneration	12	2.2 (1.2-4.2)	34% (32%-38%)	57% (55%-60%)	.01	High
Modic change	5	1.6 (0.5-5.4)	12% (10%-15%)	23% (22%-27%)	.43	High
Modic type 1 change	2	4.0 (1.1-14.6)	3% (0.7%-9%)	7% (5%-9%)	.04	Low
<i>Internal disc rupture related outcomes</i>						
Annular fissure	6	1.8 (0.97-3.3)	11% (9%-14%)	20% (18%-23%)	.06	High
High Intensity Zone	4	2.1 (0.7-6.0)	10% (7%-13%)	10% (8-13%)	.17	High
<i>Disc displacement related outcomes</i>						
Disc bulge	3	7.5 (1.3-44.6)	6% (4%-9%)	43% (38%-48%)	.03	High
Disc protrusion	9	2.7 (1.5-4.6)	19% (17%-22%)	42% (39%-45%)	.00	High
Disc extrusion	4	4.4 (2.0-9.7)	2% (0.1%-4%)	7% (5%-9%)	<.01	Low
<i>Other outcomes</i>						
Spondylolysis	2	5.1 (1.7-15.5)	2% (0%-5%)	9% (7%-12%)	<.01	Low
Spondylolisthesis	4	1.6 (0.8-3.2)	3% (2%-6%)	6% (4%-9%)	.20	Low
Central spinal canal stenosis	2	20.6 (0.1-799)	14% (10%-19%)	60% (55%-64%)	.17	High
OR=odds ratio, CI=confidence interval, Heterogeneity (I^2) was graded 'low' only for '0' values as no CI for I^2 was presented Prevalence data presented for reference only						

Table 3 Specific pathological causes of low back pain

Specific pathological causes of low back pain	Description
Vertebral fracture	<p>Symptomatic minimal trauma vertebral fractures due to osteoporosis are rare under the age of 50 years but the incidence increases rapidly with age.¹⁰¹ Although age-specific incidence is not changing, with an ageing population, the population burden is increasing. A systematic review (14 studies) found post-test probability for having a symptomatic vertebral fracture was 9% (95% CI 3–25%) for those who were older (men aged >65, women aged >75), 33% (CI 10–67%) for those with a history of prolonged corticosteroid use, and 62% (49–74%) when a contusion or abrasion was present. The probability of a minimal trauma vertebral fracture being present when multiple risk factors (at least three of female, age >70, severe trauma, and prolonged use of glucocorticoids) were present was 90% (95% CI 34–99%).³² The predictive value of such a decision rule is, however, not greatly different from clinical assessment.³⁰ Symptomatic minimal trauma vertebral fractures have been shown in some studies to have a major health impact with a mean of 158 days of limited activity and a third of those affected still have significant back pain after two years¹⁰¹ In some studies, minimal trauma vertebral fractures are also associated with a two to eight fold increased risk of mortality.¹⁰¹</p>
Axial spondyloarthritis	<p>Axial spondyloarthritis is a chronic inflammatory disease that primarily affects the axial skeleton in young people (peak of onset 20–40 years). Although traditionally considered to be a disease of young men there is only a slight male predominance in population studies.¹⁰² The term axial spondyloarthritis covers both people who have already developed structural damage in the sacroiliac joints and/or spine visible on x-rays (radiographic axial spondyloarthritis; also termed ankylosing spondylitis) and those who have not yet developed such structural damage (non-radiographic spondyloarthritis).¹⁰³ Non-radiographic spondyloarthritis is a prodrome of axial spondyloarthritis that might subsequently produce structural bony damage in the axial skeleton.¹⁰⁴ The prevalence of radiological disease is between 0.3 and 0.8% in Western countries and is dependent on the HLA-B27 prevalence in a given population.¹⁰²</p> <p>The typical presentation of axial spondyloarthritis includes morning stiffness, mostly in the lower back, with improvement observed with exercise but not with rest. In a Danish cohort of 759 people aged 18–40 years with chronic low back pain, the discriminative value of inflammatory back pain symptoms for axial</p>

	<p>spondyloarthritis was low with sensitivity and specificity ranging between 50% and 80% depending on the criteria being used.¹⁰⁵ However, around 30% of those referred to secondary care with symptoms of inflammatory back pain receive a final diagnosis of axial spondyloarthritis.¹⁰⁶ Around 5% of Europeans presenting with chronic low back pain in primary care may have axial spondyloarthritis.¹⁰⁷ There is often a delay between the onset of (back pain) symptoms and making a diagnosis of axial spondyloarthritis of five years or longer. People with axial spondyloarthritis are commonly misdiagnosed with non-specific low back pain. Since there are now effective treatments for axial spondyloarthritis, a specialist rheumatology referral is advised for people who are suspected of having an axial spondyloarthritis.</p>
Malignancy	<p>Back pain is a common symptom in people with metastatic cancer; vertebral metastases occur in 3-5% of people with cancer, and 97% of spinal tumours are metastatic disease.¹⁰⁸ Nevertheless malignancy is an uncommon cause of low back pain. Past history of malignancy is the most useful indicator for identifying malignancy in people presenting with low back pain; however it only increases the post-test probability to 7% (95% CI 3- 16%) in primary care, and to 33% (95% CI 22-46%) in the emergency setting.³² The common solid tumours metastasising to the spine are adenocarcinomas, i.e., breast, lung, prostate, thyroid and gastrointestinal. A past history of other tumours is less important. Myeloma typically presents as persistent bone pain in people aged ≥ 60.</p>
Infections	<p>Spinal infections include spondylodiscitis, vertebral osteomyelitis, epidural abscess and rarely facet joint infection. Bacterial infections are divided into pyogenic (e.g. Staphylococcus aureus and Staphylococcus epidermidis) and granulomatous diseases (e.g. tuberculosis, brucellosis). Although rare, these disorders are associated with a substantial mortality; up to 3% for epidural abscesses, 6% for spinal osteomyelitis, and possibly as high as 11% for pyogenic spondylodiscitis.¹⁰⁹⁻¹¹¹</p> <p>In high-income countries, granulomatous diseases are mainly encountered in immigrant populations; pyogenic infections are seen largely in older patients (mean age 59–69 years).¹¹² In low-income countries tuberculosis affects a broader span of ages (mean age 27–76 years), and may represent up to a third of spinal infections.¹¹² People with chronic comorbidities, particularly immunosuppressive disorders, and intravenous drug users, are at higher risk of spinal infections. Recent increases in the incidence of spinal infection are attributed to an ageing population with inherent comorbidities plus improved case ascertainment related to the availability of modern imaging techniques.^{111,113}</p>

Cauda Equina syndrome	While not strictly a cause of low back pain, cauda equina compression, which mainly arises due to disc herniation, can have catastrophic consequences. It is rare and most primary care clinicians will not see a true case in a working lifetime. ¹¹⁴ Early diagnosis and surgical treatment are probably helpful therefore there needs to be a low threshold for further assessment when there has been a new onset of perianal sensory change or bladder symptoms, or bilateral severe radicular pain with low back pain of any duration. ¹¹⁴ The cardinal clinical features are urinary retention and overflow incontinence (sensitivity 90%, specificity 95%). ¹¹⁵
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Table 4: Overview of selected predictors and their association with dichotomous outcomes of low back pain disability based on review by Chou et al⁴³

Predictor	Outcome/s Predictor scale: Association with low back pain disability	Source of evidence
Symptom related		
Previous episodes	<p>Chronic disabling pain* at 3–6 months More versus less episodes: Median LR (range) = 1.0 (0.9–1.2)</p> <p>Chronic disabling pain* at 12 months More versus less episodes: Median LR (range) = 1.1 (0.95–1.2)</p>	Systematic review including 9 longitudinal studies ⁴³
Back pain intensity	<p>Chronic disabling pain* at 3–6 months High intensity pain versus non-high: Median LR (range) = 1.7 (1.1–3.7)</p> <p>Chronic disabling pain* at 12 months High intensity pain versus non-high: Median LR (range) = 1.3 (1.2–2.0)</p>	Systematic review including 8 longitudinal studies ⁴³
Leg pain	<p>Chronic disabling pain* at 3–6 months Leg pain or radiculopathy versus no leg pain: Median LR(range) = 1.4 (1.1-1.7)</p> <p>Chronic disabling pain* at 12 months Leg pain or radiculopathy versus no leg pain: Median LR (range) = 1.4 (1.2–2.4)</p>	Systematic review including 10 longitudinal studies ⁴³
Lifestyle factors		
Body mass	<p>Chronic disabling pain* at 3–6 months BMI >25 or >27 vs lower BMI: Median LR (range) = 0.91 (0.72–1.2)</p> <p>Chronic disabling pain* at 12 months</p>	Systematic review including 3 longitudinal studies ⁴³

	BMI >25 or >27 vs lower BMI: Median LR (range) = 0.84 (0.73–0.97)	
Smoking	Chronic disabling pain* at 3–6 months Current smoker versus not: Median LR (range) = 1.2 (1.0–1.6)	Systematic review including 3 longitudinal studies ⁴³
Physical activity	Disability 1–5 years Significant association in 1/5 studies (no effect size reported)	Systematic review including 5 longitudinal studies ¹¹⁶
Psychological factors		
Depression	Mixed outcomes Significant associations with poor outcome in 8/13 cohorts OR (range) = 1.04–2.47	Systematic review including 13 longitudinal studies ¹¹⁷
Catastrophizing	Disability at 3–12 months <i>Significant association in 9/13 studies</i> High catastrophizing: OR (95% CI) = 1.56 (1.05–2.33) 0–6 scale: OR (95% CI) = 7.63 (3.70–15.74) 0–52 scale: OR (95% CI) = 1.05 (1.02–1.08) Contribution to explained variance: 0–23%	Systematic review including 13 longitudinal studies ¹¹⁸
Fear avoidance beliefs	Pain or activity limitation at 3–12 months No pooled estimates. No systematic association between fear avoidance and outcome. Poor work-related outcome at 3-12 months	Systematic review including 21 longitudinal studies ¹¹⁹

	<p>Elevated fear avoidance: OR (range) = 1.05 (95% CI 1.02–1.09) to 4.64 (95% CI 1.57–13.71) (From four studies conducted by disability insurance companies)</p> <p>Chronic disabling pain* at 3-6 months High versus no fear avoidance: Median LR(range) = 2.2 (1.5-4.9)</p> <p>Chronic disabling pain* at 12 months Median LR (range) = 2.5(2.2–2.8)</p>	<p>Systematic review including 4 longitudinal studies⁴³</p>
Social factors		
Physical work loads	<p>Chronic disabling pain* at 3–6 months Higher versus lower physical work demands: Median LR (range) = 1.2 (1.1–1.6)</p> <p>Chronic disabling pain* at 12 months Higher versus lower physical work demands: Median LR (range) = 1.4 (1.2–1.7)</p>	<p>Systematic review including 4 longitudinal studies⁴³</p>
Education	<p>Chronic disabling pain* at 3–6 months No college education or not college graduate vs more education: Median LR (range) = 1.0 (0.97–1.3)</p> <p>Chronic disabling pain* at 12 months No college education or not college graduate vs more education: Median LR (range) = 1.1 (1.1–1.2)</p>	<p>Systematic review including 10 longitudinal studies⁴³</p>

Compensation	<p>Chronic disabling pain* at 3–6 months Compensated work injury or sick leave vs not compensated work injury or sick leave: Median LR (range) = 1.3 (0.97–2.7)</p> <p>Chronic disabling pain* at 12 months Compensated work injury or sick leave vs not compensated work injury or sick leave: Median LR (range) = 1.4 (1.2 – 1.8)</p>	Systematic review including 7 longitudinal studies ⁴³
Work satisfaction	<p>Chronic disabling pain* at 3–6 months Less vs more work satisfaction: Median LR (range) = 1.1 (0.64–1.8)</p> <p>Chronic disabling pain* at 12 months Less vs more work satisfaction: Median LR (range) = 1.5 (1.3 –1.8)</p>	Systematic review including 5 longitudinal studies ⁴³
<p>LR: positive likelihood ratio, OR: odds ratio, HR: hazard ratio, CI: Confidence interval The information provided in the table provides a broad overview and was not based on a systematic review of the literature.</p>		

Table S1. Estimates of total costs, direct medical costs, and indirect societal costs, as well as cost per person in the population expressed in 2015 USD*

First authors, country	Year	Method	Total societal cost (billion)	Direct medical cost, %	Indirect societal cost, %	Total cost per person	Direct cost per person	Indirect cost per person
Maniadakis, UK ⁶	1998	Top down	26.40	15	85	449	68	381
Rizzo; ¹²⁰ Lou, ¹²¹ USA	1998	Top down	81.24	47	53	308	145	163
van Zundert, ¹²² Belgium	1999	Top down	1.93	16	84	189	30	159
Ekman ¹²³ , Sweden	2001	Top down	2.93	16	84	336	54	282
Walker ¹²⁴ , Australia	2001	Top down	11.24	11	89	583	64	518
Weiser ¹²⁵ , Switzerland	2005	Bottom up	8.92	38	62	1199	455	743
Lambeek, ⁵⁷ Netherlands	2007	Top down	4.88	12	88	300	36	264

* For each study the reported total societal costs were inflation-adjusted to 2015 US dollars based on World Bank data, divided by the total population at time of data collection, to derive the total per person cost. Based on the reported fraction of direct and indirect costs, per-person direct and indirect costs were developed.

Table S2. Relative percentage of health care costs across studies

First author, country	Year	Inpatient care	Diagnostic evaluations	Outpatient care	Physical therapy chiropractic, massage	Prescription medication
Rizzo, ¹²⁰ Lou, ¹²¹ USA	1998	38	NR*	56.0	NR	4.0
Ekman, ¹²³ Sweden	2001	12.0	NR	25.0	55.0	6.0
Walker ¹²⁴ , Australia	2001	20.0	6.7	17.4	48.2	7.5
Weiser, ¹²⁵ Switzerland	2005	37.0	5.5	24.9	31.9	1.5
Labeek ⁵⁷ , Netherlands	2007	21.0	1.0	25.0	49.0	4.0

* Not reported

Table S3. Performance and extent of validation of four low back pain prediction models

Model name (Country of development, year)	Örebro Musculoskeletal Pain Screening Questionnaire ¹²⁶ (Sweden, 1998)	STarT Back Screening Tool ¹²⁷ (UK, 2008)	The 'Hancock Rule' ¹²⁸ (Australia, 2009)
Number of items	21	9	3
Concepts covered by predictors	Pain intensity Pain frequency Episode duration Multi-site pain Activity limitation Perceived pain control Perceived risk of persistency Fear of movement Fear avoidance beliefs Anxiety Depression Sick leave Physical work exposures Work expectations Work satisfaction Sleep disturbed by pain	Bothersome pain Leg pain Multi-site pain Activity limitation Fear avoidance beliefs Anxiety Depression Catastrophizing	Pain intensity Episode duration Previous episodes
Primary outcome in development sample	Sick leave days during 6 months (0, 1-30, >30).	High disability after 6 months (at least 7 points on the Roland Morris Disability Scale).	Days to recovery from pain Discrimination based on recovery status at 11 weeks
Predictive performance in development sample	Cut-point 105 (scale 0–210): Specificity (identification of no sick leave): 0.75 Sensitivity (1–30 days): 0.86 Sensitivity (>30 days): 0.88 No overall performance measure reported	Sum scale (no cut-point): AUC (95% CI) = 0.92 (0.88–0.97)	AUC (95% CI) = 0.68 (0.56–0.80)
Predictive performance in narrow validation sample*	Cut-point 105 (scale 0–210): Specificity (identification of no sick leave): 0.81 Sensitivity (1–30 days): 0.40 Sensitivity (>30 days): 0.67 AUC (95% CI) = 0.74 (0.64–0.84)	Sum scale (no cut-point): AUC (95% CI) = 0.90 (0.88–0.93)	AUC (95% CI) for 1 week recovery = 0.65 (0.60–0.70) AUC (95% CI) for 12 week recovery = 0.60 (0.56–0.64)
Additional external validation of predictive performance	External validations have been performed in: Australia, Canada, The Netherlands, Norway, New Zealand, France (2012) ¹³⁰ Sweden (2012) ¹³¹	External validations have been performed in: UK (2012) ¹³⁴ USA (2013) ¹³⁵ Denmark (2013) Primary care ¹³⁶	N/A

Country (publication year)	China (2013) ¹³² Belgium (2012) ¹³⁰ Switzerland (2016) ¹³³ Turkey (2016) ⁸⁰ [Additional translations and psychometric testing exist]	Denmark (2014) secondary care ¹³⁷ Canada (2015) ¹³⁸ Denmark (2016) chiropractic care ¹³⁹ [Additional translations and psychometric testing exist]	
Predictive performance in external validation samples reporting Area Under the Curve Area Under the ROC Curve (95% CI)	Cut-point 113: AUC (95%CI)= 0.66 (0.52–0.81) (6 months outcome, Turkey) Sum score: AUC (95%CI)= 0.80 (0.66–0.93) (6 months outcome, Norway) AUC (95%CI)= 0.72 (0.57–0.86) (12 months outcome, Norway) AUC (95%CI)= 0.69 (0.62–0.76) (12-months outcome, China) AUC = 0.83 (6-months outcome, Belgium)	Sum score: AUC (95%CI)= 0.69 (0.66–0.73) (6 months outcome, secondary care Denmark) AUC (95%CI) = 0.71 (0.66–0.77) (6 months outcome, primary care Denmark) Three risk group: AUC (95%CI)= 0.84 (0.69–1.00) (6 months outcome, Canada) AUC (95%CI)= 0.59 (0.55–0.63) (3-months outcome, Denmark chiropractic care) AUC (95%CI)= 0.60 (0.56–0.64) (12months outcome, Denmark chiropractic care)	N/A

*validation performed by the same research team and in the same setting or in a very similar setting in the same country

Figure 1: Contributors to low back pain and disability

The model includes key contributors to low back pain and disability but does not attempt to represent the complex interactions between different contributors. *Nociceptive input includes non-identifiable sources in non-specific low back pain, neurological sources (eg, radicular pain) and specific pathology (eg, fractures).

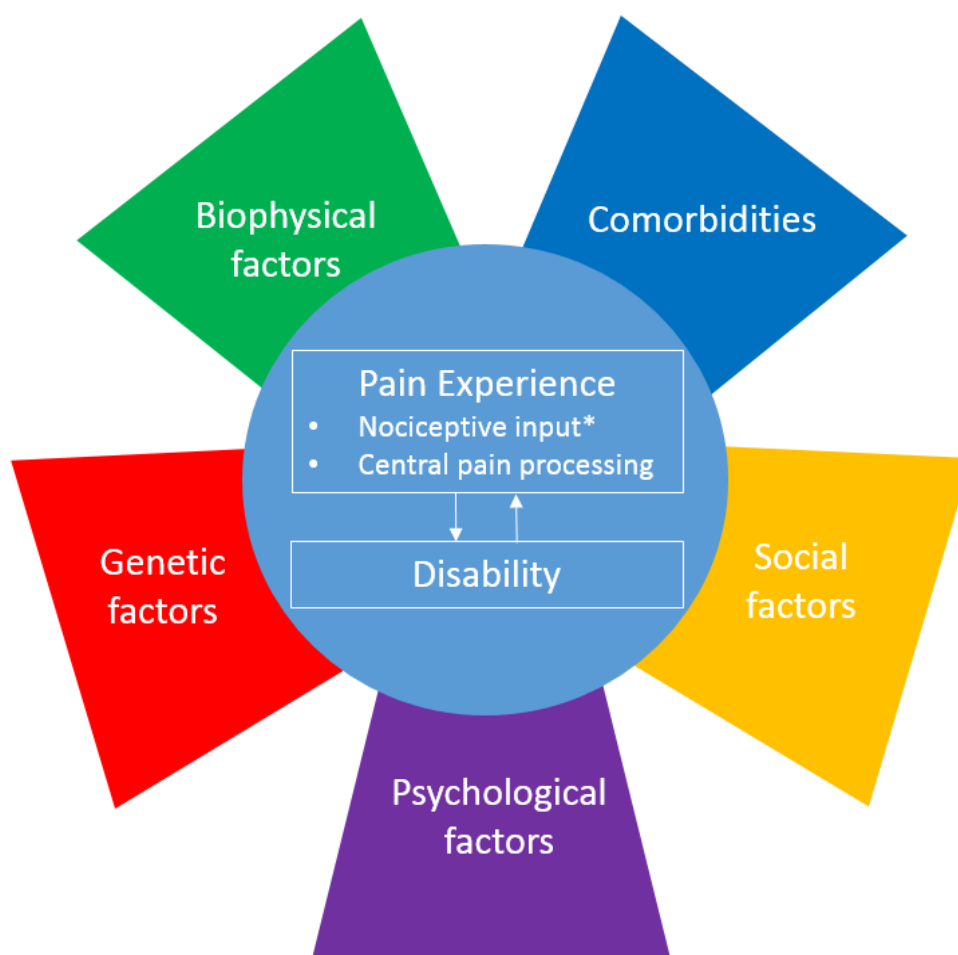


Figure 2. Median prevalence of low back pain, with interquartile range, according to sex and midpoint of age group (reprinted with permission from Hoy et al).¹

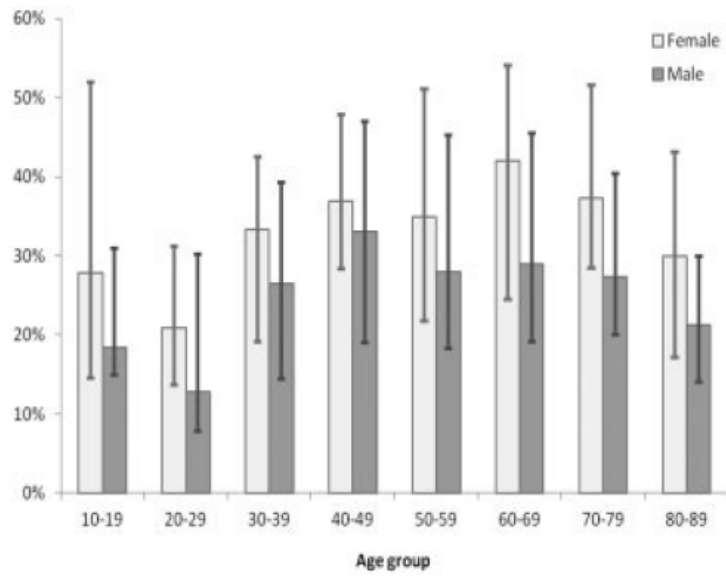
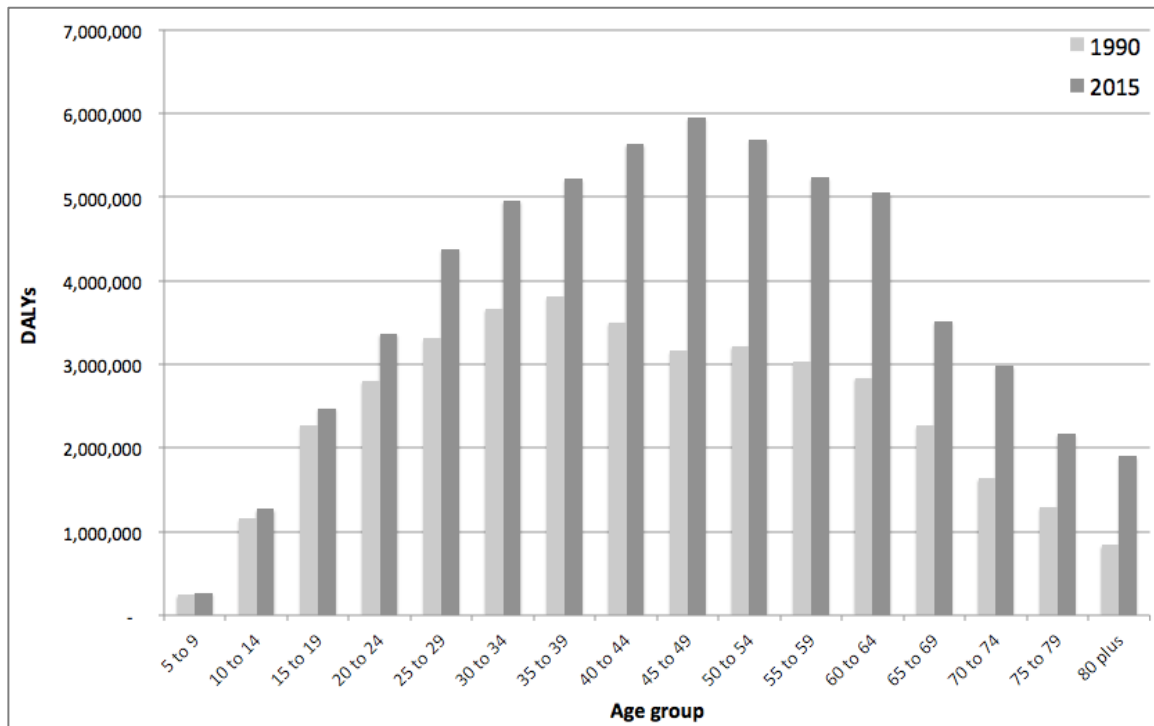


Figure 3. Median prevalence of low back pain, with interquartile range, according to sex and midpoint of age group. Midpoint = (lower limit of age group + [upper limit of age group – lower limit of age group]/2).

Figure 3: Global burden of low back pain, in Disability-Adjusted Life Years (DALYs), by age group, for 1990 and 2015 (GBD 2015).⁴¹



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