



## Low back pain 1

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

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This is the first in a [Series](#) of two papers about low back pain

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**Low back pain is a very common symptom. It occurs in high-income, middle-income, and low-income countries and all age groups from children to the elderly population. Globally, years lived with disability caused by low back pain increased by 54% between 1990 and 2015, mainly because of population increase and ageing, with the biggest increase seen in low-income and middle-income countries. Low back pain is now the leading cause of disability worldwide. For nearly all people with low back pain, it is not possible to identify a specific nociceptive cause. Only a small proportion of people have a well understood pathological cause—eg, a vertebral fracture, malignancy, or infection. People with physically demanding jobs, physical and mental comorbidities, smokers, and obese individuals are at greatest risk of reporting low back pain. Disabling low back pain is over-represented among people with low 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. Increasing evidence shows that central pain-modulating mechanisms and pain cognitions have important roles in the development of persistent disabling low back pain. Cost, health-care use, and disability from low back pain vary substantially between countries and are influenced by local culture and social systems, as well as by beliefs about cause and effect. Disability and costs attributed to low back pain are projected to increase in coming decades, in particular in low-income 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 messages

- Low back pain is an extremely common symptom in populations worldwide and occurs in all age groups, from children to the elderly population
- 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-income and middle-income countries
- Disability from low back pain is highest in working age groups worldwide, which is especially concerning in low-income 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 between 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-income and middle-income countries

### Introduction

Low back pain is an extremely common symptom experienced by people of all ages.<sup>1–3</sup> In 2015, the global point prevalence of activity-limiting low back pain was 7·3%, implying that 540 million people were affected at any one time. Low back pain is now the number one cause of disability globally.<sup>4</sup> The largest increases in disability caused by low back pain in the past few decades have occurred in low-income and middle-income countries, including in Asia, Africa, and the Middle East,<sup>5</sup> 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. 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 because it increases costs in both health-care and social supports systems.<sup>6</sup> Disability attributed to low back pain varies substantially among countries, and is influenced by social norms, local health-care approaches, and legislation.<sup>7</sup> In low-income and middle-income countries, formal and informal social-support systems are negatively affected. While 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.<sup>8</sup> Spreading high-cost health-care models to

low-income 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 two papers and a Viewpoint. 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 current treatments and promising new directions for managing low back pain is presented in paper two,<sup>9</sup> and the Viewpoint is a worldwide call to action.<sup>10</sup>

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 identified scientific studies using broad search terms in MEDLINE (PubMed) and Scopus. To identify potentially relevant papers from low-income and middle-income countries, we also searched Google Scholar and the African Index Medicus Database. To minimise selection bias and to ensure high-quality evidence was selected, systematic reviews were preferred and sought when possible. However, we also used information from large population-based cohorts, international clinical guidelines, and the Global Burden of Disease (GBD) 2015 study. Primary research from low-income and middle-income regions excluded from systematic reviews was also referenced where appropriate.

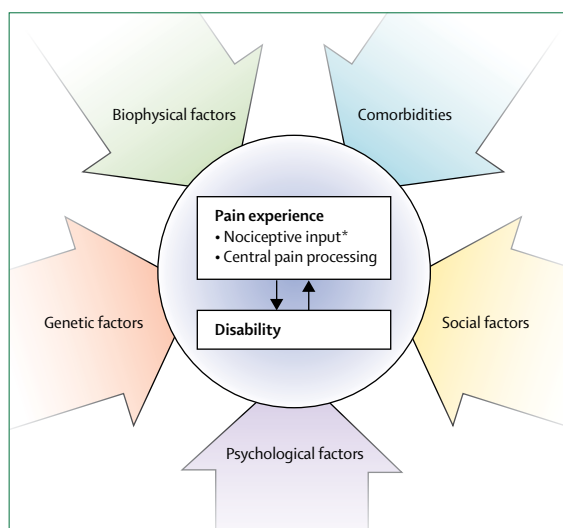
## What is low back pain?

Low back pain is a symptom not a disease, and can result from several different known or unknown abnormalities or diseases.

It is defined by the location of pain, typically between the lower rib margins and the buttock creases.<sup>11</sup> It is commonly accompanied by pain in one or both legs and some people with low back pain have associated neurological symptoms in the lower limbs.

For nearly all people presenting with low back pain, the specific nociceptive source cannot be identified and those affected are then classified as having so-called non-specific low back pain.<sup>12</sup> There are some serious causes of persistent low back pain (malignancy, vertebral fracture, infection, or inflammatory disorders such as axial spondyloarthritis) that require identification and specific management targeting the cause, but these account for a very small proportion of cases. People with low back pain often have concurrent pain in other body sites, and more general physical and mental health problems, when compared with people not reporting low back pain.<sup>13</sup> 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.<sup>13</sup> 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



**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).

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

#### Intervertebral disc

Although some imaging and clinical findings increase the likelihood that pain is arising from the intervertebral disc (with the reference standard of discography), no investigation has accurately identified a disc problem as contributing to an individual's pain;<sup>14</sup> there is no widely accepted reference standard for discogenic pain

#### Facet joint

Injecting facet joints with local anaesthetic can cause temporary relief of pain;<sup>15</sup> however, the Framingham Heart Study (3529 participants) did not find an association between radiological osteoarthritis of facet joints and presence of low back pain;<sup>16</sup> clinical identification of individuals whose facet joints are contributing to their pain is not possible.<sup>17</sup>

#### 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 might predispose to the development of Modic changes; one theory is that the pro-inflammatory response, caused by structural damage to the disc or endplate, could allow microbial infiltration, autoimmune reactions, or both, that intensify and extend nociceptor stimulation by chemical or mechanical stimuli;<sup>18</sup> a low-grade infection by *Propionibacterium acnes* might promote the development of Modic changes;<sup>19</sup> the relevance of these findings to clinical practice is, however, unclear; a systematic review concluded that Modic type 1 changes are associated with low back pain;<sup>20</sup> a subsequent study, including 1142 people, found that Modic type 2 changes were associated with disability (odds ratio 1.56, 95% CI 1.06–2.31), but not pain (1.36, 0.88–2.09);<sup>21</sup> identification of individuals in whom Modic changes are contributing to their pain is not possible.

	Number of studies	OR (95% CI)	Prevalence asymptomatic (95% CI)	Prevalence symptomatic (95% CI)	p value	Heterogeneity
<b>Intervertebral disc degeneration-related outcomes</b>						
Disc degeneration	12	2.2 (1.2-4.2)	34% (32-38)	57% (55-60)	0.01	High
Modic change	5	1.6 (0.5-5.4)	12% (10-15)	23% (22-27)	0.43	High
Modic type 1 change	2	4.0 (1.1-14.6)	3% (0.7-9)	7% (5-9)	0.04	Low
<b>Internal disc rupture-related outcomes</b>						
Annular fissure	6	1.8 (0.97-3.3)	11% (9-14)	20% (18-23)	0.06	High
High Intensity Zone	4	2.1 (0.7-6.0)	10% (7-13)	10% (8-13)	0.17	High
<b>Disc displacement-related outcomes</b>						
Disc bulge	3	7.5 (1.3-44.6)	6% (4-9)	43% (38-48)	0.03	High
Disc protrusion	9	2.7 (1.5-4.6)	19% (17-22)	42% (39-45)	0.00	High
Disc extrusion	4	4.4 (2.0-9.7)	2% (0.1-4)	7% (5-9)	<0.01	Low
<b>Other outcomes</b>						
Spondylolysis	2	5.1 (1.7-15.5)	2% (0-5)	9% (7-12)	<0.01	Low
Spondylolisthesis	4	1.6 (0.8-3.2)	3% (2-6)	6% (4-9)	0.20	Low
Central spinal canal stenosis	2	20.6 (0.1-798.8)	14% (10-19)	60% (55-64)	0.17	High

Data are modified from Brinjikji et al (2015).<sup>20</sup> Heterogeneity (*I*<sup>2</sup>) was graded "low" only for "0" values since no CI for *I*<sup>2</sup> was presented. Prevalence data presented for reference only. OR=odds ratio.

**Table 1: Strength of association between MRI findings and low back pain in younger adults**

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on both the pain experience and the associated disability (figure 1).

### Causes of 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 (panel 1).<sup>14,15</sup> Many imaging (radiography, CT scan, and MRI) findings identified in people with low back pain are also common in people without such pain, and their importance in diagnosis is a source of much debate.<sup>22</sup> Nevertheless, at least in people younger than 50 years, some MRI abnormalities are more common in those 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 (odds ratio [OR] 4.0, 95% CI 1.1-14.6), disc bulge (7.5, 1.3-44.6), disc extrusion (4.4, 2.0-9.7), and spondylolysis (5.1, 1.7-15.5; table 1).<sup>20</sup> However, evidence is insufficient to know whether MRI findings can be of use to predict the future onset, or the course, of low back pain.<sup>23</sup> Importantly, no evidence exists that imaging improves patient outcomes<sup>24</sup> and guidelines consistently recommend against the routine use of imaging for people with low back pain.<sup>25-28</sup>

### Neurological symptoms associated with low back pain

#### Radicular pain and radiculopathy

Radicular pain occurs when there is nerve-root involvement; commonly termed sciatica. The term sciatica is

used inconsistently by clinicians and patients for different types of leg or back pain and should be avoided.<sup>29</sup> 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 straining,<sup>30</sup> and straight leg raise test. Radiculopathy is characterised by the presence of weakness, loss of sensation, or loss of reflexes associated with a particular nerve root, or a combination of these, and can coexist with radicular pain. People with low back pain and radicular pain or radiculopathy are reported to be more severely affected and have poorer outcomes compared with those with low back pain only.<sup>31</sup> Disc herniation in conjunction with local inflammation is the most common cause of radicular pain and radiculopathy. Disc herniations are, however, a frequent finding on imaging in the asymptomatic population,<sup>22</sup> and they often resolve or disappear over time independent of resolution of pain.<sup>32</sup>

#### Lumbar spinal stenosis

Lumbar spinal stenosis is clinically characterised by pain or other discomfort with walking or extended standing that radiates into one or both lower limbs and is typically relieved by rest or lumbar flexion (neurogenic claudication).<sup>33</sup> It is usually 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. Expert consensus is 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.<sup>34</sup> Symptoms of lumbar spinal stenosis are thought to result from venous congestion or ischaemia of the nerve roots in the cauda equina due to compression.<sup>33</sup>

#### Specific pathological causes of low back pain

Potential causes of low back pain that might require specific treatment include vertebral fractures, inflammatory disorders (eg, axial spondyloarthritis), malignancy, infections, and intra-abdominal causes (panel 2). A study of 1172 new presentations of acute (<2 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 (eight of 11 cases), followed by inflammatory disorders (two of 11 cases).<sup>37</sup> A review from Uganda of 204 patients referred to a hospital orthopaedic clinic with a primary complaint of low back pain, showed that 4% of patients had serious spinal abnormalities due to tuberculosis, 3.5% had vertebral compression fractures, 1% brucellosis, and 1% had malignancy.<sup>52</sup> These differences in the patterns of specific pathological causes could reflect the ongoing burden of infectious diseases and their manifestations as low back pain in low-income countries. So-called red flags are case

## Panel 2: Specific pathological causes of low back pain

### Vertebral fracture

Symptomatic minimal trauma vertebral fractures due to osteoporosis are rare under the age of 50 years but the incidence increases rapidly with age.<sup>35</sup> 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 years, women aged >75 years), 33% (10–67) for those with a history of long-term 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 long-term use of glucocorticoids) were present was 90% (34–99).<sup>36</sup> The predictive value of such a decision rule is, however, not greatly different from clinical assessment.<sup>37</sup> Symptomatic minimal trauma vertebral fractures have been shown in some studies to have a major health impact with a mean of 158 days of restricted activity and a third of those affected still have significant back pain after 2 years.<sup>35</sup> In some studies, minimal trauma vertebral fractures are also associated with a two-to-eight times increased risk of mortality.<sup>35</sup>

### Axial spondyloarthritis

Axial spondyloarthritis is a chronic inflammatory disease that mainly affects the axial skeleton in young people (peak of onset 20–40 years). Although traditionally thought to be a disease of young men, there is only a slight male predominance in population studies.<sup>38</sup> The term axial spondyloarthritis covers both people who have already developed structural damage in the sacroiliac joints or spine visible, or both, on radiographs (radiographic axial spondyloarthritis; also termed ankylosing spondylitis) and those who have not yet developed such structural damage (non-radiographic spondyloarthritis).<sup>39</sup> Non-radiographic spondyloarthritis is a prodrome of axial spondyloarthritis that might subsequently produce structural bony damage in the axial skeleton.<sup>40</sup> 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.<sup>38</sup>

The typical presentation of axial spondyloarthritis includes morning stiffness, mostly in the lower back, with improvement seen 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 spondyloarthritis was low with sensitivity and specificity ranging between 50% and 80% depending on the criteria being used.<sup>41</sup> However, around 30% of those referred to secondary care with symptoms of inflammatory back pain receive a final diagnosis of axial spondyloarthritis.<sup>42</sup> Around 5% of European people presenting with chronic low back pain in primary care could have axial spondyloarthritis.<sup>43</sup> There is often a delay between the onset of (back pain) symptoms and making a diagnosis of axial spondyloarthritis of 5 years or longer. People

with axial spondyloarthritis are commonly misdiagnosed with non-specific low back pain. Since effective treatments are now available for axial spondyloarthritis, a specialist rheumatology referral is advised for people who are suspected of having an axial spondyloarthritis.

### Malignancy

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.<sup>44</sup> Nevertheless, malignancy is an uncommon cause of low back pain. Past history of malignancy is the most useful indicator for identifying such disease 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% (22–46) in the emergency setting.<sup>36</sup> The common solid tumours metastasising to the spine are adenocarcinomas—ie, 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 years and older.

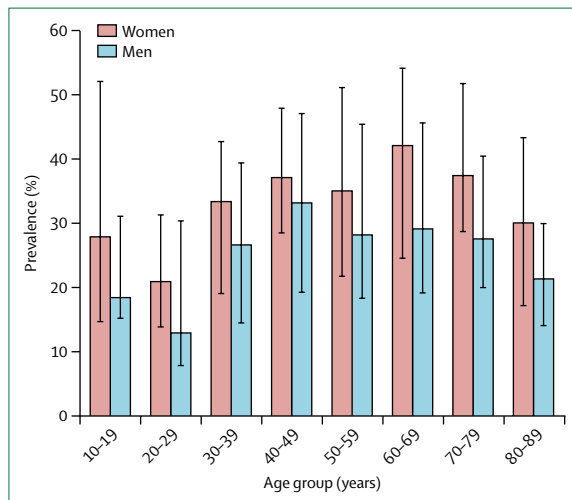
### Infections

Spinal infections include spondylodiscitis, vertebral osteomyelitis, epidural abscess, and rarely facet joint infection. Bacterial infections are divided into pyogenic (eg, *Staphylococcus aureus* and *S epidermidis*) and granulomatous diseases (eg, 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.<sup>45–47</sup> 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).<sup>48</sup> In low-income countries, tuberculosis affects a broader span of ages (mean age 27–76 years), and could represent up to a third of spinal infections.<sup>48</sup> 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.<sup>47,49</sup>

### Cauda equina syndrome

Although not strictly a cause of low back pain, cauda equina compression, which mainly arises from disc herniation, can have catastrophic consequences. It is rare and most primary care clinicians will not see a true case in a working lifetime.<sup>50</sup> 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.<sup>50</sup> The cardinal clinical features are urinary retention and overflow incontinence (sensitivity 90%, specificity 95%).<sup>51</sup>





**Figure 2: Median prevalence of low back pain, with IQR, according to sex and midpoint of age group, reproduced from Hoy et al<sup>1</sup> with permission from John Wiley and Sons**

history or clinical findings believed to increase the risk of a serious disease; however, 80% of people with acute low back pain have at least one red flag despite less than 1% having a serious disorder.<sup>37</sup> Nearly all recommended individual red flags are uninformative and do not substantially change post-test probabilities of a serious abnormality.<sup>36</sup> The very low specificity of most red flags contributes to unnecessary specialist referrals and imaging.<sup>33</sup> 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.<sup>53</sup> The US guideline for imaging advises deferral of imaging pending a trial of therapy when there are weak risk factors for cancer or axial spondyloarthritis.<sup>54</sup>

### 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 high-income, medium-income, and low-income countries report having had low back pain.<sup>55,56</sup> Most adults will have low back pain at some point.<sup>57</sup> The median 1-year period prevalence globally in the adult population is around 37%, it peaks in mid-life, and is more common in women than in men (figure 2).<sup>1</sup> Low back pain that is accompanied by activity limitation increases with age.<sup>58</sup> The mean prevalence in high-income countries is higher than in middle-income and low-income countries (32.9% [SD 19.0] vs 25.4% [25.4] vs 16.7% [16.7]), but globally there is no difference between rural and urban areas.<sup>1</sup> 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 in working population than in non-working

populations for reasons that are not clear.<sup>59</sup> The gender pattern in low-income and middle-income regions might also differ from that of high-income countries and even differ between low-income regions. For example, men seem to report low back pain more often than women in Africa.<sup>56</sup> This was not the case in Latin America,<sup>60</sup> which might reflect African culture, in which men often do hard physical labour, as well as gender inequalities, which might result in women under-reporting their low back pain.

## Burden and impact of low back pain

### Overall disability

The 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 worldwide.<sup>61</sup> Low back pain was responsible for around 60.1 million years lived with disability (YLD) in 2015, an increase of 54% since 1990.<sup>4</sup> It is the number one cause of disability globally, as well as in 14 of the 21 GBD world regions.<sup>4</sup> Less than 28% of prevalent cases (n=151 million) fell in the severe and most severe categories; however, these cases accounted for 77% of all disability caused by low back pain (46.5 million YLDs).<sup>62</sup> Thus, most people with 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 2). The overall increase in the global burden of low back pain is almost entirely due to population increase and ageing in both high-income, low-income and middle-income countries, as opposed to increased prevalence.<sup>1,68</sup>

### Work disability

Disability from low back pain is highest in working age groups worldwide (figure 3),<sup>4,61</sup> which is especially concerning in low-income 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.<sup>69</sup> 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 limitation.<sup>70</sup> A survey among 500 farmers in rural Nigeria showed that more than half reduced their farming workload because of low back pain.<sup>71</sup> Thus, disability associated with low back pain might 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

Outcomes (predictor scale: association with low back pain disability)		Source of evidence
<b>Symptom-related factors</b>		
Previous episodes	Chronic disabling pain* at 3–6 months; more vs less episodes: median LR 1.0 (range 0.9–1.2); chronic disabling pain* at 12 months; more vs less episodes: median LR 1.1 (range 0.95–1.2)	Systematic review including nine longitudinal studies <sup>63</sup>
Back pain intensity	Chronic disabling pain* at 3–6 months; high intensity pain vs non-high: median LR 1.7 (range 1.1–3.7); chronic disabling pain* at 12 months; high intensity pain vs non-high: median LR 1.3 (range 1.2–2.0)	Systematic review including eight longitudinal studies <sup>63</sup>
Presence of leg pain	Chronic disabling pain* at 3–6 months; leg pain or radiculopathy vs no leg pain: median LR 1.4 (range 1.1–1.7); chronic disabling pain* at 12 months; leg pain or radiculopathy vs no leg pain: median LR 1.4 (range 1.2–2.4)	Systematic review including ten longitudinal studies <sup>63</sup>
<b>Lifestyle factors</b>		
Body mass	Chronic disabling pain* at 3–6 months; BMI >25 or >27 vs lower BMI: median LR 0.91 (range 0.72–1.2); chronic disabling pain* at 12 months; BMI >25 or >27 vs lower BMI: median LR 0.84 (range 0.73–0.97)	Systematic review including three longitudinal studies <sup>63</sup>
Smoking	Chronic disabling pain* at 3–6 months; current smoker vs not: median LR 1.2 (range 1.0–1.6)	Systematic review including three longitudinal studies <sup>63</sup>
Physical activity	Disability 1–5 years; significant association in one of five studies (no effect size reported)	Systematic review including five longitudinal studies <sup>64</sup>
<b>Psychological factors</b>		
Depression	Mixed outcomes; significant associations with poor outcome in eight of 13 cohorts; OR (range) 1.04–2.47	Systematic review including 13 longitudinal studies <sup>65</sup>
Catastrophising	Disability at 3–12 months; significant association in nine of 13 studies; high catastrophising: OR 1.56 (95% CI 1.05–2.33); 0–6 scale: 7.63 (3.70–15.74); 0–52 scale: 1.05 (1.02–1.08); contribution to explained variance: 0–23%	Systematic review including 13 longitudinal studies <sup>66</sup>
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; elevated fear avoidance: OR (range) 1.05 (95% CI 1.02–1.09) to 4.64 (1.57–13.71; from four studies done by disability insurance companies); chronic disabling pain* at 3–6 months; high vs no fear avoidance: median LR 2.2 (range 1.5–4.9); chronic disabling pain* at 12 months; median LR 2.5 (range 2.2–2.8)	Systematic review including 21 longitudinal studies <sup>67</sup> Systematic review including four longitudinal studies <sup>63</sup>
<b>Social factors</b>		
Physical work loads	Chronic disabling pain* at 3–6 months; higher vs lower physical work demands: median LR 1.2 (range 1.1–1.6); chronic disabling pain* at 12 months; higher vs lower physical work demands: median LR 1.4 (range 1.2–1.7)	Systematic review including four longitudinal studies <sup>63</sup>
Education	Chronic disabling pain* at 3–6 months; no college education or not college graduate vs more education: median LR 1.0 (range 0.97–1.3); chronic disabling pain* at 12 months; no college education or not college graduate vs more education: median LR 1.1 (range 1.1–1.2)	Systematic review including ten longitudinal studies <sup>63</sup>
Compensation	Chronic disabling pain* at 3–6 months; compensated work injury or sick leave vs not compensated work injury or sick leave: median LR 1.3 (range 0.97–2.7); chronic disabling pain* at 12 months; compensated work injury or sick leave vs not compensated work injury or sick leave: median LR 1.4 (range 1.2–1.8)	Systematic review including seven longitudinal studies <sup>63</sup>
Work satisfaction	Chronic disabling pain* at 3–6 months; less vs more work satisfaction: median LR 1.1 (range 0.64–1.8); chronic disabling pain* at 12 months; less vs more work satisfaction: median LR 1.5 (range 1.3–1.8)	Systematic review including five longitudinal studies <sup>63</sup>
The information provided in the table provides a broad overview and was not based on a systematic review of the literature. LR=positive likelihood ratio. BMI=body-mass index. OR=odds ratio. HR=hazard ratio. *Pain persistent beyond 3 months and at least moderately affecting ability to work or function.		

**Table 2: Overview of selected predictors and their association with dichotomous outcomes of low back pain disability**

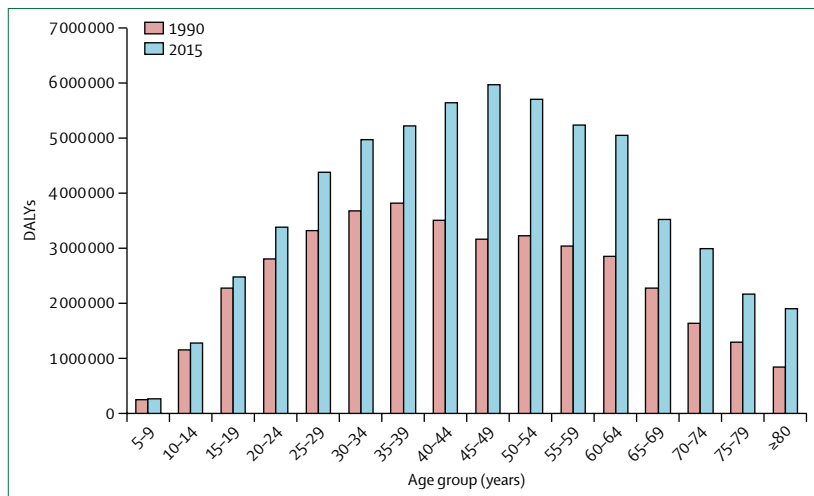
exposure or individual factors, are largely responsible for national differences in the rates and extent of work disability attributed to low back pain.<sup>7</sup> In Europe, low back pain is the most common cause of medically certified sick leave and early retirement.<sup>72</sup> However, work disability due to low back pain varies substantially 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% and 6.4%, respectively), but the rate of longer-term medically certified sickness absence was very different (22% and 15%, respectively).<sup>73</sup> In the USA, low back pain accounts for more lost workdays than any other occupational musculoskeletal condition,<sup>74</sup> but although 58 of 10000 US workers filed a back-related claim in 1999, the comparable figure from Japan during the same year was only one of 10000.<sup>75</sup>

### Social identity and inequality

The effect of low back pain on social identity and inequality is substantial worldwide. Ethnographic interviews of villagers in Botswana found 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.<sup>76</sup>

Froud and colleagues<sup>77</sup> reviewed 42 qualitative studies all from high-income countries, and found that many people living with low back pain struggled to meet their social expectations and obligations and that achieving them might then threaten the credibility of their suffering, with disability claims being endangered. Although those with back pain seek to achieve pre-morbid levels of health, many find with time that this aim is unrealistic and live with reduced expectations.<sup>77</sup> Likewise, MacNeela and colleagues<sup>78</sup> reviewed 38 separate qualitative studies, also from high-income countries, and found some common themes, including: 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),



**Figure 3: Global burden of low back pain, in disability-adjusted life-years (DALYs), by age group, for 1990 and 2015**

Data are from the Global Health Data Exchange.

For the **Global Health Data Exchange** see <http://ghdx.healthdata.org/gbd-2016>

coming to terms with the pain, and learning self-management strategies.

Globally, low back pain contributes to inequality. In low-income and middle-income countries, poverty and inequality might increase as participation in work is affected. Furthermore, formal return-to-work systems are often not in place, and workers might be retrenched, placing more strain on family and community livelihoods.<sup>69</sup> In Australia, Schofield and colleagues<sup>79</sup> found that individuals who exit the workforce early as a result of their low back pain have substantially less wealth by age 65 years, even after adjustment for education. The median value of accumulated wealth for those who retire early because of low back pain is only AUS\$5038 by the time they reach 65 years of age, compared with \$339121 for those who remain in the workforce.<sup>79</sup>

### Cost of low back pain

No relevant studies on costs associated with low back pain from low-income and middle-income countries were identified. Costs associated with low back pain are generally reported as direct medical (health-care) costs, and indirect (work absenteeism or productivity loss) costs. Only a few studies have reported other direct non-medical 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 (appendix). 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.<sup>6</sup> Replacement wages account for 80–90% of total costs, and consistently a small percentage of cases account for these.<sup>80</sup> Some of the observed

variation in costs for low back pain over time might 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 after a change in legislation that reduced disability pensions and applied evidence-based criteria for medical practices.<sup>7,81</sup>

Estimates of direct medical costs associated with low back pain are also all from high-income countries, with the USA having the highest costs, attributable to a more medically intensive approach and higher rates of surgery compared with other high-income countries (appendix).<sup>8,82</sup> 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 10000 registered persons),<sup>83</sup> and in South Africa, low back pain is the sixth most common complaint seen in primary health care.<sup>84</sup> In addition to conventional medicine, complementary and alternative medical approaches are popular with people who have low back pain. For example, in the USA 44% of the population used at least one complementary or alternative health-care therapy in 1997;<sup>85</sup> and the most common reason was low back pain.<sup>86</sup>

### Natural history

Low back pain is increasingly understood as a long-lasting condition with a variable course rather than episodes of unrelated occurrences.<sup>87</sup> Around half the people seen with low back pain in primary care have a trajectory of continuing or fluctuating pain of low-to-moderate intensity, some recover, and some have persistent severe low back pain.<sup>88</sup> A systematic review<sup>89</sup> (33 cohorts; 11166 participants) provides strong evidence that most episodes of low back pain improve substantially within 6 weeks, and by 12 months average pain levels are low (6 points on a 100-point scale; 95% CI 3–10). However, two-thirds of patients still report some pain at 3 months; 67% (95% CI 50–83) and 12 months; 65% (54–75).<sup>89,90</sup> Recurrences of low back pain are common but a 2017 systematic review (seven studies; 1780 participants) found that research does not provide robust estimates of the risk of low back pain recurrence. The best evidence suggests around 33% of people will have a recurrence within 1 year of recovering from a previous episode.<sup>91</sup>

### Risk factors and triggers for episodes of low back pain

Although the impact of low back pain in low-income and middle-income countries on systems and people differs from high-income countries, there seem to be fewer fundamental differences in the risk factors between regions. A systematic review<sup>92</sup> (eight cohorts; 5165 participants) found consistent evidence that people who have had previous episodes of low back pain are at increased risk of a new episode. Likewise, people with other chronic conditions, including asthma, headache, and diabetes, are more likely to report low back pain

See [Online](#) for appendix

than people in good health (pooled ORs 1.6–4.2).<sup>93</sup> People with poor mental health are also at increased risk. For example, a UK cohort study<sup>94</sup> (5781 participants) found psychological distress at age 23 years predicted incident low back pain 10 years later (OR 2.52, 95% CI 1.65–3.86). The Canadian National Population Health Survey<sup>95</sup> with 9909 participants found that pain-free individuals with depression were more likely to develop low back pain within 2 years than were people without depression (OR 2.9, 95% CI 1.2–7.0). Mechanisms behind the coexistence of low back pain and other chronic diseases are not known, but systematic reviews of cohort studies indicate that lifestyle factors such as smoking,<sup>96</sup> obesity,<sup>97,98</sup> and low levels of physical activity<sup>99</sup> 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<sup>93</sup> (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. A comprehensive genetic epidemiological analysis of 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 might indicate a common genetic basis for a high proportion of spinal pain.<sup>100</sup>

An Australian case-crossover study (999 participants) showed that awkward postures (OR 8.0, 95% CI 5.5–11.8), heavy manual tasks (5.0, 3.3–7.4), feeling tired (3.7, 2.2–6.3), or being distracted during an activity (25.0, 3.4–184.5) were all associated with increased risk of a new episode of low back pain.<sup>101</sup> 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 in low-income and middle-income countries.<sup>56,60</sup> A systematic review (25 cohorts) showed 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).<sup>102</sup> The existence of a causal pathway between these risk factors and low back pain, however, remains unclear.<sup>103</sup>

### Multifactorial contributors to persistent disabling low back pain

In recent decades, the biopsychosocial model has been applied as a framework for understanding the complexity of low back pain disability 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 2). However, no firm boundaries exist among these factors and they all interact with each other. Thus, persistent disabling low back pain is not merely

a result of nociceptive input. Although there are substantially fewer data from low-income and middle-income countries than from high-income countries, the available data suggest similar multifactorial contributors seem to be important in all countries.<sup>104</sup>

### Biophysical factors

Although 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 might have alterations in muscle size,<sup>105</sup> composition,<sup>106</sup> and coordination<sup>107</sup> that differ from those without pain. These changes could be more than merely a direct consequence of pain and are only partly affected by psychological factors.<sup>108</sup>

### Psychological factors

Psychological factors are often investigated separately, but there is a substantial overlap of constructs such as depression, anxiety, catastrophising (ie, an irrational belief that something is far worse than it really is), and self-efficacy (ie, belief in one's ability to influence events affecting one's life). 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 2). For example, in a UK cohort study of 531 participants, pain-related distress explained 15% and 28% of the variance in pain and disability, respectively.<sup>109</sup> 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 model 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 have a central role in the development and maintenance of disability, and more so than the pain itself.<sup>110</sup> A systematic review, including 12 mediation studies, identified self-efficacy, psychological distress, and fear as intermediate factors explaining some of the pathway between having neck or back pain and developing disability.<sup>111</sup> 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.<sup>112</sup> Therefore, some chronic pain treatments have shifted away from aiming to directly alleviate pain to aiming to change beliefs and behaviours.<sup>113</sup>

### Social and societal factors

Chronic disabling low back pain affects people with low income and short education disproportionately. In a UK study of 2533 people, life-time socioeconomic status



predicted disability due to any pain condition in older age (independent of comorbid conditions, psychological indicators and body-mass index (BMI); OR 2.04 (95% CI 1.55–2.68).<sup>114</sup> Cross-sectional data from the USA (National Health Interview Survey 2009–10, 5103 people) found that those with persistent low back pain were more likely to have had less than high-school education (2.27, 1.53–3.38) and had an annual household income of less than US\$20 000 (2.29, 1.46–3.58).<sup>115</sup> Suggested mechanisms for the effect of low education on back pain include environmental and lifestyle exposures in lower socioeconomic groups, lower health literacy, and health care not being available or adequately targeted to people with low education.<sup>116</sup> Also, being in routine and manual occupations and having increased physical workloads is associated with disabling low back pain (table 2).

#### Central pain processing and modulation

Nociceptive input is processed throughout the nervous system, including modulation within the spinal cord and supraspinal centres. In chronic pain, supraspinal centres 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 patient.<sup>117</sup> A systematic review (27 studies; 1037 participants) identified moderate evidence that patients with chronic low back pain show structural brain differences in specific cortical and subcortical areas, and altered functional connectivity in pain-related areas following painful stimulation.<sup>118</sup> The clinical implication of these findings remains to be clarified.<sup>117</sup>

#### 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, which have been developed to identify people at particular risk of developing disabling low back pain (appendix). 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.<sup>119</sup>

#### Limitations

Despite advances in many aspects of understanding low back pain, including the burden, course, risk factors, and causes, some important limitations exist. Most evidence comes from high-income countries, and may or may not generalise to low-income and middle-income countries. Although many factors are associated with both the development of low back pain and the transition to persistent disabling pain, the underlying mechanisms, including the effect of co-occurring non-communicable diseases, are poorly understood. Despite

the burden of low back pain, research is often not a priority in low-income and middle income countries, and thus the consequences of low back pain in these settings are largely unknown. The functional domains used in the GBD 2015 study do not take into account broader aspects of life, such as participation, well-being, social identity, carer burden, use of health-care resources, and work disability costs. In cost studies, a top-down approach is most often used and those might 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-income and middle-income countries, which 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 increased 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 few people end up with persistent disabling pain affected 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 substantially between countries, and are related to social norms, health-care approaches, and legislation. Although there are several global initiatives to address the global burden of low back pain as a public health problem, there is a need to identify cost-effective and context-specific strategies for managing low back pain to mitigate the consequences of the current and projected future burden.

#### Contributors

JH and MU were part of the 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 contributed to all sections of the paper and edited it for key intellectual content. JH, MJH, AK, JK, MLF, SG, RJS, 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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#### Declaration of interests

See appendix for authors' declaration of interests.

#### References

- Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum* 2012; **64**: 2028–37.
- Kamper SJ, Henschke N, Hestbaek L, Dunn KM, Williams CM. Musculoskeletal pain in children and adolescents. *Braz J Phys Ther* 2016; **16**: 10.
- Hartvigsen J, Christensen K, Frederiksen H. Back pain remains a common symptom in old age: a population-based study of 4486 Danish twins aged 70–102. *Eur Spine J* 2003; **12**: 528–34.
- Global Burden of Disease, Injury Incidence, Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; **388**: 1545–602.
- Hoy DG, Smith E, Cross M, et al. Reflecting on the global burden of musculoskeletal conditions: lessons learnt from the global burden of disease 2010 study and the next steps forward. *Ann Rheum Dis* 2015; **74**: 4–7.
- Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain* 2000; **84**: 95–103.
- Anema JR, Schellart AJ, Cassidy JD, Loisel P, Veerman TJ, van der Beek AJ. Can cross country differences in return-to-work after chronic occupational back pain be explained? An exploratory analysis on disability policies in a six country cohort study. *J Occup Rehabil* 2009; **19**: 419–26.
- Deyo RA, Mirza SK, Turner JA, Martin BI. Overtreating chronic back pain: time to back off? *J Am Board Fam Med* 2009; **22**: 62–68.
- Foster NE, Anema JR, Cherkin D, et al. Prevention and treatment of low back pain: evidence, challenges, and promising directions. *Lancet* 2018; published online March 21. [http://dx.doi.org/10.1016/S0140-6736\(18\)30489-6](http://dx.doi.org/10.1016/S0140-6736(18)30489-6).
- Buchbinder R, van Tulder M, Öberg B, et al. Low back pain: a call for action. *Lancet* 2018; published online March 21. [http://dx.doi.org/10.1016/S0140-6736\(18\)30488-4](http://dx.doi.org/10.1016/S0140-6736(18)30488-4).
- Dionne CE, Dunn KM, Croft PR, et al. A consensus approach toward the standardization of back pain definitions for use in prevalence studies. *Spine* 2008; **33**: 95s103.
- Maher C, Underwood M, Buchbinder R. Non-specific low back pain. *Lancet* 2017; **389**: 736–47.
- Hartvigsen J, Natvig B, Ferreira M. Is it all about a pain in the back? *Best Pract Res Clin Rheum* 2013; **27**: 613–23.
- Hancock MJ, Maher CG, Latimer J, et al. Systematic review of tests to identify the disc, SIJ or facet joint as the source of low back pain. *Eur Spine J* 2007; **16**: 1539–50.
- Maas ET, Ostelo RW, Niemisto L, et al. Radiofrequency denervation for chronic low back pain. *Cochrane Database Syst Rev* 2015: CD008572.
- Kalichman L, Li L, Kim DH, et al. Facet joint osteoarthritis and low back pain in the community-based population. *Spine* 2008; **33**: 2560–65.
- Maas ET, Juch JN, Ostelo RW, et al. Systematic review of patient history and physical examination to diagnose chronic low back pain originating from the facet joints. *Eur J Pain* 2017; **21**: 403–14.
- Dudli S, Fields AJ, Samartzis D, Karppinen J, Lotz JC. Pathobiology of Modic changes. *Eur Spine J* 2016; **25**: 3723–34.
- Dudli S, Liebenberg E, Magnitsky S, Miller S, Demir-Deviren S, Lotz JC. Propionibacterium acnes infected intervertebral discs cause vertebral bone marrow lesions consistent with Modic changes. *J Orthop Res* 2016; **34**: 1427–55.
- Brinjikji W, Diehn FE, Jarvik JG, et al. MRI Findings of disc degeneration are more prevalent in adults with low back pain than in asymptomatic controls: a systematic review and meta-analysis. *Am J Neuroradiol* 2015; **36**: 2394–99.
- Maatta JH, Karppinen J, Paananen M, et al. Refined phenotyping of Modic changes: imaging biomarkers of prolonged severe low back pain and disability. *Medicine* 2016; **95**: e3495.
- Brinjikji W, Luetmer PH, Comstock B, et al. Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. *Am J Neuroradiol* 2015; **36**: 811–16.
- Steffens D, Hancock MJ, Maher CG, Williams C, Jensen TS, Latimer J. Does magnetic resonance imaging predict future low back pain? A systematic review. *Eur J Pain* 2014; **18**: 755–65.
- Jarvik JG, Gold LS, Comstock BA, et al. Association of early imaging for back pain with clinical outcomes in older adults. *JAMA* 2015; **313**: 1143–53.
- Wong JJ, Cote P, Sutton DA, et al. Clinical practice guidelines for the noninvasive management of low back pain: A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMA) Collaboration. *Eur J Pain* 2016; **21**: 201–16.
- Stochkendahl MJ, Kjaer P, Hartvigsen J, et al. National clinical guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy. *Eur Spine J* 2018; **27**: 60–75.
- Bernstein IA, Malik Q, Carville S, Ward S. Low back pain and sciatica: summary of NICE guidance. *BMJ* 2017; **356**: i6748.
- Qaseem A, Wilt TJ, McLean RM, Forciea MA, for the Clinical Guidelines Committee of the American College of Physicians. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2017; **166**: 514–30.
- Lin CW, Verwoerd AJ, Maher CG, et al. How is radiating leg pain defined in randomized controlled trials of conservative treatments in primary care? A systematic review. *Eur J Pain* 2014; **18**: 455–64.
- Verwoerd AJ, Mens J, El Barzouhi A, Peul WC, Koes BW, Verhagen AP. A diagnostic study in patients with sciatica establishing the importance of localization of worsening of pain during coughing, sneezing and straining to assess nerve root compression on MRI. *Eur Spine J* 2016; **25**: 1389–92.
- Kongsted A, Kent P, Jensen TS, Albert H, Manniche C. Prognostic implications of the Quebec Task Force classification of back-related leg pain: an analysis of longitudinal routine clinical data. *BMC Musculoskelet Dis* 2013; **14**: 171.
- Chiu CC, Chuang TY, Chang KH, Wu CH, Lin PW, Hsu WY. The probability of spontaneous regression of lumbar herniated disc: a systematic review. *Clin Rehabil* 2015; **29**: 184–95.
- Chad DA. Lumbar spinal stenosis. *Neurol Clin* 2007; **25**: 407–18.
- Tomkins-Lane C, Melloh M, Lurie J, et al. Consensus on the clinical diagnosis of lumbar spinal stenosis: results of an international Delphi study. *Spine* 2016; **41**: 1239–46.
- Schousboe JT. Epidemiology of vertebral fractures. *J Clin Densitom* 2016; **19**: 8–22.
- Downie A, Williams CM, Henschke N, et al. Red flags to screen for malignancy and fracture in patients with low back pain: systematic review. *BMJ* 2013; **347**: f7095.
- Henschke N, Maher CG, Refshauge KM, et al. Prevalence of and screening for serious spinal pathology in patients presenting to primary care settings with acute low back pain. *Arthritis Rheum* 2009; **60**: 3072–80.
- Stolwijk C, van Onna M, Boonen A, van Tubergen A. The global prevalence of spondyloarthritis: A systematic review and meta-regression analysis. *Arthritis Care Res* 2015; **68**: 1320–31.
- Rudwaleit M, van der Heijde D, Landewe R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009; **68**: 777–83.
- Sieper J, van der Heijde D. Review: Nonradiographic axial spondyloarthritis: new definition of an old disease? *Arthritis Rheum* 2013; **65**: 543–51.

- 41 Arnbak B, Hendricks O, Horslev-Petersen K, et al. The discriminative value of inflammatory back pain in patients with persistent low back pain. *Scand J Rheumatol* 2016; **45**: 321–28.
- 42 Poddubnyy D, van Tubergen A, Landewe R, Sieper J, van der Heijde D. Defining an optimal referral strategy for patients with a suspicion of axial spondyloarthritis: what is really important? *Ann Rheum Dis* 2015; **74**: e69.
- 43 van Hooft L, Luime J, Han H, Vergouwe Y, Weel A. Identifying axial spondyloarthritis in Dutch primary care patients, ages 20–45 years, with chronic low back pain. *Arthritis Care Res* 2014; **66**: 446–53.
- 44 Lewandowski K, Anderson M, McLain R. Tumors of the Spine. In: Herkowitz H, Garfin S, Eismont F, Bell G, Balderston R, eds. *Rothman-Simeone the spine*. Philadelphia, PA: Elsevier Saunders; 2011: 1480–512.
- 45 Schoenfeld AJ, Wahlquist TC. Mortality, complication risk, and total charges after the treatment of epidural abscess. *Spine J* 2015; **15**: 249–55.
- 46 Fantoni M, Trecarichi EM, Rossi B, Mazzotta V, Di Giacomo G, Nasto LA, Di Meco E, Pola E. Epidemiological and clinical features of pyogenic spondylodiscitis. *Eur Rev Med Pharmacol Sci* 2012; **16**: 2–7.
- 47 Akiyama T, Chikuda H, Yasunaga H, Horiguchi H, Fushimi K, Saita K. Incidence and risk factors for mortality of vertebral osteomyelitis: a retrospective analysis using the Japanese diagnosis procedure combination database. *BMJ Open* 2013; **3**: e002412.
- 48 Trecarichi EM, Di Meco E, Mazzotta V, Fantoni M. Tuberculous spondylodiscitis: epidemiology, clinical features, treatment, and outcome. *Eur Rev Med Pharmacol Sci* 2012; **16**: 58–72.
- 49 Kehrer M, Pedersen C, Jensen TG, Lassen AT. Increasing incidence of pyogenic spondylodiscitis: a 14-year population-based study. *J Infect* 2014; **68**: 313–20.
- 50 Lavy C, James A, Wilson-MacDonald J, Fairbank J. Cauda equina syndrome. *BMJ* 2009; **338**: b936.
- 51 Abraham JL. Assessment and treatment of patients with malignant spinal cord compression. *J Support Oncol* 2004; **2**: 88–91.
- 52 Galukande M, Muwazi S, Mugisa DB. Aetiology of low back pain in Mulago Hospital, Uganda. *Afr Health Sci* 2005; **5**: 164–67.
- 53 Underwood M, Buchbinder R. Red flags for back pain. *BMJ* 2013; **347**: f7432.
- 54 American Academy of Family Physicians. Imaging for Low Back Pain 2017 <http://www.aafp.org/patient-care/clinical-recommendations/all/cw-back-pain.html> (accessed Nov 1, 2017).
- 55 Calvo-Munoz I, Gomez-Conesa A, Sanchez-Meca J. Prevalence of low back pain in children and adolescents: a meta-analysis. *BMC Pediatrics* 2013; **13**: 14.
- 56 Louw QA, Morris LD, Grimmer-Somers K. The prevalence of low back pain in Africa: a systematic review. *BMC Musculoskelet Disord* 2007; **8**: 105.
- 57 Lemeunier N, Leboeuf-Yde C, Gagey O. The natural course of low back pain: a systematic critical literature review. *Chiropract Man Ther* 2012; **20**: 33.
- 58 Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014; **73**: 968–74.
- 59 Jackson T, Thomas S, Stabile V, Shotwell M, Han X, McQueen K. A Systematic review and meta-analysis of the global burden of chronic pain without clear etiology in low- and middle-income countries: trends in heterogeneous data and a proposal for new assessment methods. *Anesth Analg* 2016; **123**: 739–48.
- 60 Garcia JB, Hernandez-Castro JJ, Nunez RG, et al. Prevalence of low back pain in Latin America: a systematic literature review. *Pain Phys* 2014; **17**: 379–91.
- 61 Global Burden of Disease 2015 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; **388**: 1603–58.
- 62 Global Burden of Disease 2015 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015; **386**: 2145–91.
- 63 Chou R, Shekelle P. Will this patient develop persistent disabling low back pain? *JAMA* 2010; **303**: 1295–302.
- 64 Hendrick P, Milosavljevic S, Hale L, et al. The relationship between physical activity and low back pain outcomes: a systematic review of observational studies. *Eur Spine J* 2011; **20**: 464–74.
- 65 Pinheiro MB, Ferreira ML, Refshauge K, et al. Symptoms of depression as a prognostic factor for low back pain: a systematic review. *Spine J* 2016; **16**: 105–16.
- 66 Wertli MM, Eugster R, Held U, Steurer J, Kofmehl R, Weiser S. Catastrophizing—a prognostic factor for outcome in patients with low back pain: a systematic review. *Spine J* 2014; **14**: 2639–57.
- 67 Wertli MM, Rasmussen-Barr E, Weiser S, Bachmann LM, Brunner F. The role of fear avoidance beliefs as a prognostic factor for outcome in patients with nonspecific low back pain: a systematic review. *Spine J* 2014; **14**: 816–36.
- 68 Hoy D, March L, Brooks P, Woolf A, Blyth F, Vos T, Buchbinder R. Measuring the global burden of low back pain. *Best Pract Res Clin Rheum* 2010; **24**: 155–65.
- 69 Lucchini RG, London L. Global occupational health: current challenges and the need for urgent action. *Ann Glob Health* 2014; **80**: 251–56.
- 70 Jelsma J, Mielke J, Powell G, De Weerd W, De Cock P. Disability in an urban black community in Zimbabwe. *Disabil Rehabil* 2002; **24**: 851–59.
- 71 Fabunmi AA, Aba SO, Odunaiya NA. Prevalence of low back pain among peasant farmers in a rural community in South West Nigeria. *Afr J Med Med Sci* 2005; **34**: 259–62.
- 72 Bevan S, Quadrello T, McGee R, Mahdon M, Vavrovsky A, Barham L. Fit For work? Musculoskeletal disorders in the European workforce: fit For work Europe: The Work Foundation, 2009.
- 73 Ihlebaek C, Hansson TH, Laerum E, et al. Prevalence of low back pain and sickness absence: a “borderline” study in Norway and Sweden. *Scand J Public Health* 2006; **34**: 555–58.
- 74 US Bone & Joint Initiative. The Burden of Musculoskeletal Diseases in the United States, 2014. <http://www.boneandjointburden.org/about/rights> (accessed Nov, 2017).
- 75 Volinn E, Nishikitani M, Volinn W, Nakamura Y, Yano E. Back pain claim rates in Japan and the United States: framing the puzzle. *Spine* 2005; **30**: 697–704.
- 76 Hondras M, Hartvigsen J, Myburgh C, Johannessen H. Everyday burden of musculoskeletal conditions among villagers in rural Botswana: a focused ethnography. *J Rehabil Med* 2016; **48**: 449–55.
- 77 Froud R, Patterson S, Eldridge S, et al. A systematic review and meta-synthesis of the impact of low back pain on people’s lives. *BMC Musculoskelet Disord* 2014; **15**: 50.
- 78 MacNeela P, Doyle C, O’Gorman D, Ruane N, McGuire BE. Experiences of chronic low back pain: a meta-ethnography of qualitative research. *Health Psychol Rev* 2015; **9**: 63–82.
- 79 Schofield D, Kelly S, Shrestha R, Callander E, Passey M, Percival R. The impact of back problems on retirement wealth. *Pain* 2012; **153**: 203–10.
- 80 Hashemi L, Webster BS, Clancy EA. Trends in disability duration and cost of workers’ compensation low back pain claims (1988–1996). *J Occup Environ Med* 1998; **40**: 1110–19.
- 81 Lambeek LC, van Tulder MW, Swinkels IC, Koppes LL, Anema JR, van Mechelen W. The trend in total cost of back pain in The Netherlands in the period 2002 to 2007. *Spine* 2011; **36**: 1050–58.
- 82 Hansson TH, Hansson EK. The effects of common medical interventions on pain, back function, and work resumption in patients with chronic low back pain: a prospective 2-year cohort study in six countries. *Spine* 2000; **25**: 3055–64.
- 83 Jordan KP, Kadam UT, Hayward R, Porcheret M, Young C, Croft P. Annual consultation prevalence of regional musculoskeletal problems in primary care: an observational study. *BMC Musculoskelet Disord* 2010; **11**: 144.
- 84 Mash B, Fairall L, Adejayan O, et al. A morbidity survey of South African primary care. *PLoS One* 2012; **7**: e32358.
- 85 Wolsko P, Ware L, Kutner J, et al. Alternative/complementary medicine: wider usage than generally appreciated. *J Altern Complement Med* 2000; **6**: 321–26.
- 86 Wolsko PM, Eisenberg DM, Davis RB, Kessler R, Phillips RS. Patterns and perceptions of care for treatment of back and neck pain: results of a national survey. *Spine* 2003; **28**: 292–97.
- 87 Dunn KM, Hestbaek L, Cassidy JD. Low back pain across the life course. *Best Pract Res Clin Rheum* 2013; **27**: 591–600.

- 88 Kongsted A, Kent P, Axen I, Downie AS, Dunn KM. What have we learned from ten years of trajectory research in low back pain? *BMC Musculoskelet Dis* 2016; **17**: 220.
- 89 da C Menezes Costa L, Maher CG, Hancock MJ, McAuley JH, Herbert RD, Costa LO. The prognosis of acute and persistent low-back pain: a meta-analysis. *CMAJ* 2012; **184**: E613–24.
- 90 Itz CJ, Geurts JW, van Kleef M, Nelemans P. Clinical course of non-specific low back pain: a systematic review of prospective cohort studies set in primary care. *Eur J Pain* 2013; **17**: 5–15.
- 91 da Silva T, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of recurrence of low back pain: a systematic review. *J Orthop Sports Phys Ther* 2017; **47**: 305–13.
- 92 Taylor JB, Goode AP, George SZ, Cook CE. Incidence and risk factors for first-time incident low back pain: a systematic review and meta-analysis. *Spine J* 2014; **14**: 2299–319.
- 93 Ferreira PH, Beckenkamp P, Maher CG, Hopper JL, Ferreira ML. Nature or nurture in low back pain? Results of a systematic review of studies based on twin samples. *Eur J Pain* 2013; **17**: 957–71.
- 94 Power C, Frank J, Hertzman C, Schierhout G, Li L. Predictors of low back pain onset in a prospective British study. *Am J Public Health* 2001; **91**: 1671–78.
- 95 Currie SR, Wang J. More data on major depression as an antecedent risk factor for first onset of chronic back pain. *Psychol Med* 2005; **35**: 1275–82.
- 96 Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between smoking and low back pain: a meta-analysis. *Am J Med* 2010; **123**: 87.
- 97 Zhang TT, Liu Z, Liu YL, Zhao JJ, Liu DW, Tian QB. Obesity as a risk factor for low back pain: a meta-analysis. *Clin Spine Surg* 2016; **31**: 22–27.
- 98 Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol* 2010; **171**: 135–54.
- 99 Shiri R, Falah-Hassani K. Does leisure time physical activity protect against low back pain? Systematic review and meta-analysis of 36 prospective cohort studies. *Br J Sports Med* 2017; **51**: 1410–18.
- 100 Hartvigsen J, Nielsen J, Kyvik KO, et al. Heritability of spinal pain and consequences of spinal pain: a comprehensive genetic epidemiologic analysis using a population-based sample of 15,328 twins ages 20–71 years. *Arthritis Rheum* 2009; **61**: 1343–51.
- 101 Steffens D, Ferreira ML, Latimer J, et al. What triggers an episode of acute low back pain? A case-crossover study. *Arthritis Care Res* 2015; **67**: 403–10.
- 102 Heneweer H, Staes F, Aufdemkampe G, van Rijn M, Vanhees L. Physical activity and low back pain: a systematic review of recent literature. *Eur Spine J* 2011; **20**: 826–45.
- 103 Kwon BK, Roffey DM, Bishop PB, Dagenais S, Wai EK. Systematic review: occupational physical activity and low back pain. *Occup Med* 2011; **61**: 541–48.
- 104 Oncu J, Iliser R, Kuran B. Cross-cultural adaptation of the Orebro Musculoskeletal Pain Questionnaire among Turkish workers with low back pain. *J Back Musculoskelet Rehabil* 2016; **29**: 135–43.
- 105 Goubert D, Oosterwijk JV, Meeus M, Danneels L. Structural changes of lumbar muscles in non-specific low back pain: a systematic review. *Pain Phys* 2016; **19**: E985–1000.
- 106 Sions JM, Elliott JM, Pohlig RT, Hicks GE. Trunk muscle characteristics of the multifidi, erector spinae, psoas, and quadratus lumborum in older adults with and without chronic low back pain. *J Orthop Sports Phys Ther* 2017; **47**: 173–79.
- 107 Hodges PW, Richardson CA. Inefficient muscular stabilization of the lumbar spine associated with low back pain. A motor control evaluation of transversus abdominis. *Spine* 1996; **21**: 2640–50.
- 108 Dubois JD, Abboud J, St-Pierre C, Piche M, Descarreaux M. Neuromuscular adaptations predict functional disability independently of clinical pain and psychological factors in patients with chronic non-specific low back pain. *J Electromyogr Kinesiol* 2014; **24**: 550–57.
- 109 Campbell P, Bishop A, Dunn KM, Main CJ, Thomas E, Foster NE. Conceptual overlap of psychological constructs in low back pain. *Pain* 2013; **154**: 1783–91.
- 110 Crombez G, Eccleston C, Van Damme S, Vlaeyen JW, Karoly P. Fear-avoidance model of chronic pain: the next generation. *Clin J Pain* 2012; **28**: 475–83.
- 111 Lee H, Hubscher M, Moseley GL, et al. How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain* 2015; **156**: 988–97.
- 112 Jackson T, Wang Y, Wang Y, Fan H. Self-efficacy and chronic pain outcomes: a meta-analytic review. *J Pain* 2014; **15**: 800–14.
- 113 Frost H, Klaber Moffett JA, Moser JS, Fairbank JC. Randomised controlled trial for evaluation of fitness programme for patients with chronic low back pain. *BMJ* 1995; **310**: 151–54.
- 114 Lacey RJ, Belcher J, Croft PR. Does life course socio-economic position influence chronic disabling pain in older adults? A general population study. *Eur J Public Health* 2013; **23**: 534–40.
- 115 Shmigel A, Foley R, Ibrahim H. Epidemiology of chronic low back pain in US adults: National Health and Nutrition Examination Survey 2009–2010. *Arthritis Care Res* 2016; **68**: 1688–94.
- 116 Dionne CE, Von Korff M, Koepsell TD, Deyo RA, Barlow WE, Checkoway H. Formal education and back pain: a review. *J Epidemiol Community Health* 2001; **55**: 455–68.
- 117 Roussel NA, Nijs J, Meeus M, Mylius V, Fayt C, Oostendorp R. Central sensitization and altered central pain processing in chronic low back pain: fact or myth? *Clin J Pain* 2013; **29**: 625–38.
- 118 Kregel J, Meeus M, Malfliet A, et al. Structural and functional brain abnormalities in chronic low back pain: A systematic review. *Semin Arthritis Rheum* 2015; **45**: 229–37.
- 119 Kent PM, Keating JL. Can we predict poor recovery from recent-onset nonspecific low back pain? A systematic review. *Man Ther* 2008; **13**: 12–28.

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