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Evidence-informed management of chronic low back pain with back schools, brief education, and fear-avoidance training

Jens Ivar Brox, MD, PhD[a,f,*], Kjersti Storheim, PT, PhD[b], Margreth Grotle, PT, PhD[c], Torill H. Tveito, PhD[d], Aage Indahl, MD, PhD[e], Hege R. Eriksen, PSY, PhD[f]

[a]*Orthopedic Department, Rikshospitalet University, 0027 Oslo, Norway*
[b]*Orthopedic Center, Ullevål University Hospital and Norwegian Research Center for Active Rehabilitation, Oslo, Norway*
[c]*National Resource Center for Rehabilitation in Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*
[d]*Department of Education and Health Promotion, University of Bergen, Norway*
[e]*Hospital of Rehabilitation, Stavern, Norway*
[f]*Department of Education and Health Promotion, University of Bergen and Unifob Health, Norway*

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Abstract **EDITORS' PREFACE:** The management of chronic low back pain (CLBP) has proven very challenging in North America, as evidenced by its mounting socioeconomic burden. Choosing among available nonsurgical therapies can be overwhelming for many stakeholders, including patients, health providers, policy makers, and third-party payers. Although all parties share a common goal and wish to use limited health-care resources to support interventions most likely to result in clinically meaningful improvements, there is often uncertainty about the most appropriate intervention for a particular patient. To help understand and evaluate the various commonly used nonsurgical approaches to CLBP, the North American Spine Society has sponsored this special focus issue of *The Spine Journal*, titled Evidence-Informed Management of Chronic Low Back Pain Without Surgery. Articles in this special focus issue were contributed by leading spine practitioners and researchers, who were invited to summarize the best available evidence for a particular intervention and encouraged to make this information accessible to nonexperts. Each of the articles contains five sections (description, theory, evidence of efficacy, harms, and summary) with common subheadings to facilitate comparison across the 24 different interventions profiled in this special focus issue, blending narrative and systematic review methodology as deemed appropriate by the authors. It is hoped that articles in this special focus issue will be informative and aid in decision making for the many stakeholders evaluating nonsurgical interventions for CLBP.

Keywords: Chronic low back pain; Back school; Physiotherapy; Fear avoidance; Patient education

Description

History

The Swedish Back School was introduced by Zachrisson-Forssell in 1969, based on knowledge about the intervertebral disc, spinal anatomy and physiology, and ergonomics [1,2]. Patients were initially taught how to protect spinal structures in daily activities and back exercises were later added to back school [3]. Back schools were eventually incorporated into comprehensive multidisciplinary programs for chronic low back pain (CLBP) [4].

Waddell attempted to construct a new theoretic framework for the treatment of low back pain (LBP) [5] based on his observations that the natural history and epidemiology of LBP suggest it is benign and self-limiting. Traditional approaches based on the medical model of disease were contrasted with a biopsychosocial model of illness to reexamine success and failure in management of LBP. This shift in thoughts regarding LBP inspired others to reconsider its management. For example, Indahl et al. began telling patients that light activity would not further injure

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* Corresponding author. Orthopedic Department, Rikshospitalet University Hospital, 0027 Oslo, Norway. Tel.: (47) 23-076029.

E-mail address: jens.ivar.brox@rikshospitalet.no (J.I. Brox)

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their discs or other structures [6]. A clinical examination was supplemented by brief education given by a physiatrist, physiotherapist, or nurse; during which patients were instructed that the worst thing they could do to their back was to be too careful. The link between emotions and CLBP was attributed to increased tension in the muscles. Brief education has also been managed in the physiotherapy setting [7,8]. Cherkin et al. evaluated the value of an educational booklet in patients with acute LBP [9], which was not effective in reducing symptoms, disability, or health-care use. His findings challenged the value of purely educational approaches in reducing symptoms and costs of LBP.

Lethem et al. introduced the fear-avoidance model in 1983, and a questionnaire for measurement of fear-avoidance beliefs was published by Waddell et al. in 1993 [10,11]. The central concept of this model is fear of pain, which was further outlined by Vlaeyen and Linton in 2000 [12], who postulated that confrontation and avoidance are the two extreme responses to this fear. Whereas the former leads to reduction of fear over time, the latter leads to maintenance and exacerbation of fear, which may generate a phobic state in CLBP. Several studies have shown that physical performance and self-reported disability are associated with cognitive and behavioral aspects of pain, in addition to sensory and biomedical ones [13–17]. Behavior that is believed to be caused by fear of movement is commonly observed among persons with CLBP who have been told or experienced that the ''wrong movement'' might cause a serious problem and should be avoided, which may increase the risk of prolonged disability [15,18].

Subtypes

Several interventions have similar goals for CLBP, including back schools, brief education, and fear-avoidance training. Although presented as different types of treatment, it should be noted that there is considerable overlap among these approaches. However, categorizing these interventions will increase the homogeneity among studies reviewed and improve the precision of our recommendations.

General description

Back schools can be defined as an intervention consisting of group education, training, and exercises, delivered by a physiotherapist or other health provider. Back schools are often organized in an occupational setting or may be part of a multidisciplinary rehabilitation program. Brief education involves only short contact with health-care professionals through patient-led self-management groups, educational booklets, and on-line discussion groups [19]. These interventions often encourage self-management, provide advice to stay active, and reduce potential concerns about LBP. Fear-avoidance training as an intervention encourages a return to normal activities and physical exercise to address fear avoidance, or kinesiophobia, which can be assessed by validated questionnaires [11,20,21].

Practitioner, setting, and availability

Many health providers may deliver basic back school interventions with additional content-specific training, including physiotherapists, physicians, occupational therapists, or chiropractors. A trained mental health professional such as a psychologist or psychiatrist may be required for advanced fear-avoidance training. The qualifications and training required for brief educations vary considerably, and are similar to those for back schools. These interventions occur in occupational settings or private practices of health providers. These interventions are available in the United States, mostly in larger cities.

Reimbursement

Pertinent CPT (US reimbursement) codes include 90804: Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in an office or outpatient facility, approximately 20 to 30 minutes face to face with the patient or 90805: Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in an office or outpatient facility, approximately 20 to 30 minutes face to face with the patient; with medical evaluation and management services; other codes apply to longer visits. Most insurers will reimburse brief education administered by a licensed health provider, but may require documentation before approving more intensive, lengthy, and costly fear-avoidance training programs.

Theory

Mechanism of action

The word doctor comes from the Latin word docere (to teach) and underscores the importance of communication in the health provider/patient relationship. Although most usual health consultations contain an element of education, this aspect is often minimized in favor of other interventions. When dealing with a complex disorder such as CLBP, education is essential to reassure patients that severity of pain is not an indication of disease severity. It should also encourage beneficial thoughts and actions, discourage impediments to recovery, and outline realistic treatment goals and expectations. Educational aspects are especially important therapies when other therapies are not effective or have a delayed onset. Patients with CLBP often fail to discuss their fears with health providers for many reasons, including fear of receiving unfavorable answers to their questions, dislike of further questioning by health providers in response to their fears, or worry that their fears will be belittled. Negative test results for serious pathology have great power to reassure the patient only if their significance is carefully explained.

Back schools typically teach about spinal anatomy and ergonomics to encourage protection of the spinal structures, though the impact of this information on patients' fear has not been addressed. Cherkin et al. reported that although knowledge about the spine was improved following back schools, the effect on pain and disability was sparse compared with other treatments in patients with acute LBP [9].

Behavior that derives from pain avoidance is inhibitory and may contribute to chronicity and even learned helplessness [22]. At present, we do not know whether this inhibition leads to a gradual development of depression, with its low psychomotor level in all dimensions. Automated movements are unconscious, but may be brought to conscious analysis and observation in patients with CLBP, which occupies more brain capacity and reduces physical performance. If CLBP is viewed as a threatening situation, anxious persons will give priority to thoughts and information related to their fear.

The cognitive activation theory of stress attempts to explain how pain leads to neurophysiological activation and has proposed that a stress alarm occurs when there is a discrepancy between what is expected and what is experienced by the individual [23]. Although the discrepancy is not an immediate threat to their health, a sustained state of related anxiety may lead to CLBP through established pathophysiological responses. The challenge in patients with CLBP is to balance information and expectancies regarding spinal structures and the adoption of pain behavior. A positive response outcome expectancy (eg, coping) may reduce the stress response and negative response outcome expectancy (eg, hopelessness) may increase the risk of sustained activation. Interventions such as back school, brief education, and fear avoidance may improve CLBP by increasing knowledge, which in turn decreases false expectations, lending to fewer instances of discrepancies in experience.

Diagnostic testing required

Most patients with CLBP should have a thorough history and clinical examination to rule out serious pathology. The simple and practical classification of CLBP into three categories (specific spinal pathology, nerve root involvement, and nonspecific mechanical disorder) sets the priority in the clinical examination.

Indications and contraindications

These interventions are used mainly for nonspecific, mechanical CLBP. The interventions evaluated have not included patients who have serious somatic or psychiatric comorbidity that may require tailored psychological care (eg, cognitive behavioral therapy [CBT]). The ideal CLBP patients for each of these interventions are briefly described below, based on the authors' clinical experience.

Back schools

The ideal patient is middle aged, suffers from yearly recurrent episodes of moderate LBP, has been out of work for short periods yearly, reports that sitting and standing for more than half an hour is not comfortable, complains of pain and stiffness in the morning, avoids lifting, is comfortable while walking, but avoids jogging, and though medication and manipulation have relieved symptoms for short periods, they do not prevent recurrences.

Brief education

The ideal patient is a young manual laborer enjoys his job but has been out of work for less than 8 weeks (his first time out of work). Although he has a normal range of motion, he moves carefully in an attempt to avoid pain, and back muscles are tense and painful. Magnetic resonance imaging reveals a small disc protrusion, which is not believed to cause his pain or functional limitations. Medication, massage, and acupuncture have not improved symptoms or decreased disability.

Fear-avoidance training

The ideal patient has moderate-to-severe pain, is unable to participate in ordinary physical activity, and has been told to avoid bending, jumping, lifting, and playing golf and tennis. Clinical examination reveals that all movements are painful and limited though neurological examination has not shown any signs of nerve root involvement. Magnetic resonance imaging has revealed disc degeneration and bulging of the two lower segments. A comprehensive examination reveals that the patient has poor physical tests and high scores on fear-avoidance beliefs for physical activity. Standard conservative care has not been helpful and the patient is considered a potential candidate for spinal fusion.

Evidence of efficacy

Review methods

A computerized search of medical databases was undertaken, combining condition-specific search terms recommended by the Cochrane Back Review Group (CBRG) with the words "back school," "patient education," "information," "pain management," "fear avoidance," "kinesiophobia," and "pain-related fear." Additional randomized controlled trials (RCTs) were identified from reference lists and the authors' personal knowledge of the literature.

Studies in which most of the patients had pain for less than 12 weeks were excluded. Likewise, studies on patients with CLBP with a select or uniform pathology (eg, spondylolisthesis or postoperative pain) were excluded. Most studies included patients with both CLBP and lower limb pain, unless pain was of true radicular nature. Back schools were included when given to groups of patients by a paramedical or physiotherapist or medical specialist, and if the back

schools constituted the main part of the intervention. Brief education was included if the intervention consisted of up to four sessions and constituted the main part of the intervention. Fear-avoidance training was included if the training was a separate intervention or part of a rehabilitation program. In addition, pain-related fear had to be measured before and after the intervention.

Effectiveness was based on pain, disability, sick leave, recurrence, cost effectiveness, or use of health-care resources; variables such as range of motion or muscle strength were not considered. Two authors independently assessed the methodological quality of each study. In the case of disagreement, a third independent member evaluated the study to reach consensus. Previously evaluated studies were assessed only if there was a disagreement between previous quality evaluations. Authors did not evaluate RCTs on which they were authors. The methodological quality of a systematic review (SR) identified by the search was assessed using the Oxman & Guyatt index. SRs were rated from 0 to 7, with a rating of 5 or higher were considered to be of high quality [24].

RCTs not included in SRs were assessed for their methodological quality using 11 criteria related to internal validity of the trial, awarding 1 point for each condition (5 or more was considered high quality) [25] (Table 1). Recommendations given for each treatment were based on the strength of evidence, cost effectiveness, and duration of the effect, using a modified grading system proposed in the European Guidelines [19] (Tables 2 and 3).

Systematic reviews

Back schools

We identified seven SRs [19,26–31], including two CBRG reviews, the latest of which reviewed 21 reports of 12 RCTs published before November 2004 [26]. Back schools had been compared with waiting-list controls or placebo interventions in eight trials and with other conservative treatments (exercises, spinal or joint manipulation, myofascial therapy, and instructions/advice) in six trials in patients with CLBP. Six RCTs were conducted in the occupational setting. The Cochrane review concluded that most of the RCTs were of low methodological quality, and there was moderate evidence that back schools conducted in the occupational setting (as opposed to patients from the general population or primary/secondary care) were more effective than other treatments, placebo, or waiting-list controls for pain, functional status, and return to work during short- and intermediate-term follow-up.

The latest published SR included the same studies but reached different conclusions [19]. The authors reported conflicting evidence for the effectiveness of back schools with regard to pain, functional status, and return to work, compared with waiting-list controls or placebo interventions. They also noted that back schools were more effective than other treatments to which they were compared with regard to short-term, but not long-term, effects on pain and disability.

Brief education

One SR including 12 RCTs was identified [19]. It was concluded that there is moderate evidence that brief education are better than usual care in reducing sick leave and disability and as effective as routine physiotherapy and aerobic exercise in reducing disability. The SR found limited or conflicting evidence that Internet-based interventions are more effective than no intervention and as effective as massage and acupuncture in reducing pain and disability.

Fear-avoidance training

No SRs or meta-analysis were found.

Table 1
Criteria used to assess methodical quality of included studies

1	Adequate method of randomization
2	Concealment of treatment allocation
3	Withdrawal/drop-out rate described and acceptable
4	Co-interventions avoided or equal
5	Blinding of patients
6	Blinding of observer
7	Blinding of care provider
8	Intention-to-treat analysis
9	Compliance
10	Similarity of baseline characteristics

Table 2
Levels of evidence

Level	Evidence	Supporting evidence
A	Strong	Generally, consistent findings provided by (a systematic review of) multiple high-quality RCTs.
B	Moderate	Generally, consistent findings provided by (a systematic review of) multiple (at least four) low-quality RCTs, or at least two high-quality RCTs.
C	Limited	One RCT (either of low or high quality) or inconsistent findings from (a systematic review of) multiple (at least four) RCTs.
D	None	No RCTs

RCT=randomized controlled trial.

Table 3
Recommendations

Recommendation	Supporting evidence
Recommended	Level A/B evidence of effectiveness in relation to control treatments or usual care and as good as other recommended treatments, by example exercises, was required.
Consider using	As for recommended treatment, but with some concerns regarding the comparison with other recommended treatments, duration of the effect, or cost effectiveness.
Cannot recommend	Level C/D evidence regarding effectiveness.
Do not recommend	Level A/B evidence of effectiveness that the intervention is less effective than usual care.

Randomized controlled trials

Back schools

We excluded six of the RCTs that had been included in previous SRs summarized above for the following reasons: two consisted of a comprehensive multidisciplinary program [4,32]; one was a comprehensive behavioral program [33]; one assessed the additional effectiveness of social intercourse [34]; one did not properly report differences between groups [35]; and one was written in German [36]. Two RCTs published after November 2004 were also identified [32,37], though one was excluded because the study evaluated a comprehensive multidisciplinary program [32].

Our review included eight studies with 1,002 patients (Table 4) [3,37–43]; one trial had two reports with a later follow-up at 3 years [44]. Physiotherapists were involved in all studies. In addition, a physician or a paramedical therapist was involved in six studies. Three of the included studies were of high quality [3,37,43]. Recurrence was reported in three studies comparing back schools with usual care or no intervention [37,42,43]. Recurrence was reduced in one high-quality study [43], while back school was less effective than exercise in one study [42]. Pain was compared with waiting list, placebo or no intervention in five RCTs, and exercises in one study. Pain was reduced at short-term follow-up in one study [39], and at long-term follow-up in one RCT [43]. Disability was reported in seven studies, and was improved compared with no intervention in two studies [39,43], and with usual care and a cognitive behavioral-based back school in one study [37]. Sick leave was reported as an outcome in five studies, and reduced in one high-quality study [43].

Brief education

We excluded one of the RCTs previously included in SRs and reported in two papers because it evaluated the effectiveness of additional physiotherapy [7,8]. We also identified seven additional RCTs reported in eight papers [45–52]. Four trials were excluded for the following reasons: one assessed the additional effect of stabilizing exercises and manipulation [47,49]; one evaluated the additional effect of yoga [51]; one did not report group comparisons [46]; and one because 75% of the patients had back pain less than 4 weeks [45].

Our review included 11 studies with 3,357 patients reported in 13 papers [6,48,50,52–62], of which 7 were high quality (Table 5) [6,48,50,56,59,60].

Five RCTs [6,55,56,59,60], including four of high quality, evaluated brief education in the clinical setting consisting of examination, information, reassurance, and advice to stay active. All these studies—except one—were conducted in the hospital setting and both a physician (physiatrist) and a physiotherapist were involved. One high-quality study evaluated the effect of neurophysiology education, including presentation of the nervous system, how nerves communicate, and the adaptability of the nervous system [48]. Pain was not reduced in any of the five studies, but pain attitudes were reduced in one RCT (Table 2). Disability was reduced in three of the five studies. The reduction was observed only at one of four end points in one [55], and was, according to the authors of no clinical significance in another [48]. Sick leave was reported as an outcome in four high-quality studies, and reduced in three [6,56,60].

Five studies, two of high quality, evaluated back book or Internet interventions [50,52,53,58,62]. Pain was reported in all studies, with conflicting evidence. Disability was reported in four studies and results were also conflicting. Sick leave was not reported as an outcome.

Fear-avoidance training

Six high-quality RCTs including 380 patients reported in seven papers were identified (Table 6) [63–69]. A psychologist in four of the studies gave the intervention. Three experimental trials were small, had a crossover design, and reported that exposure in vivo was more effective in reducing fear avoidance, pain, and disability than graded activity [63–65]. One large trial found that an intervention in a primary care and physiotherapy setting incorporating fear-reducing techniques was more effective than usual care in reducing pain-related fear, pain, disability, and return to work [67].

Two trials published in three papers compared a rehabilitation program consisting of cognitive intervention and exercises with spinal fusion including postoperative rehabilitation [66,68,69]. Fear-avoidance training was one component of the rehabilitation program and emphasized exposure to physical activities labeled not recommended. The cognitive intervention and exercise was more effective than fusion in reducing fear avoidance, and equal to fusion in reducing pain, disability, and return to work.

Ongoing studies

A protocol exists for a planned CBRG review on fear-avoidance training.

Harms

The side effects and adverse events related to these interventions are unknown.

Summary

Back schools

There is conflicting evidence that back schools are not effective in reducing recurrences of LBP compared with usual care or no intervention, and limited evidence that back schools are less effective than exercises. We found moderate evidence that back schools are not better than waiting list, any intervention, placebo, or exercises for reduction of pain. We found conflicting evidence that back schools are not better than waiting list, any intervention, or placebo for reduction of disability, and limited evidence that back school is better

Table 4
Back schools

Reference Country Participants	Setting Profession involved	Intervention	Duration/frequency	Effectiveness	Quality rating
[38] Netherlands n=43	Primary care PT	Swedish Back School (I) vs. placebo (detuned shortwave) (C)	I and C: 4×1 h for 2 wk	Pain and disability, 4 and 16 wk: I=C Sick leave: not reported	Low
[3] UK n=92 (78)*	Hospital outpatient orthopedic clinic PT and occupational therapist	Swedish Back School including exercises (I) vs. three sessions with exercises and a back care leaflet (C)	I: 3×1.5 h in 1 wk C: 3×0.5 h in 1 wk	Pain and disability, 6 wk: I=C and 16 wk: I=C Sick leave: not reported	High
[39] Finland n=188 (females)	Rehabilitation department PT and physician	Swedish Back School including exercises (I) vs. no intervention (C)	I: 6×1 h in 3 wk+2 classes after 6 mo	Pain, 6 mo: I>C and 12 mo: I=CDisability, 6 and 12 mo: I>C Sick leave, 6 and 12 mo: I=C	Low
[40] Switzerland n=80	Hospital PT and invited lecturers**	Maastricht Back School including training of skills (I) vs. waiting list (C)	I: 7×2.5 h+1 class after 8 wk	Pain, disability, and sick leave, posttreatment: I=C	Low
[41] Switzerland n=77	Hospital PT and invited lecturers**	Maastricht Back School including training of skills (I) vs. waiting list (C)	I: 7×2.5 h+1 class after 8 wk	Pain, disability, and sick leave, 2 and 6 mo: I=C	Low
[42] Israel n=142	Hospital PT and physical education instructor	Back school in groups of 10–12 people (I) vs. flexion and extension exercises in groups of 10–12 people (C1) vs. no intervention (C2)	I: 4×1.5 h in 2 wk+1 class after 2 mo C1: 24×3/4 h; 2 times weekly for 3 mo	Recurrence: 3, 6, and 12 mo: I<C1, I=C2 Pain, disability, and sick leave: not reported.	Low
[43] Norway n=81	Physical therapy in primary care	Back school including practical training and exercises (I) vs. no intervention (C)	I: 20×1 h (20 min education+40 min practical training and exercises) for 13 wk	Recurrence: 5 mo, 1 and 3 y: I>C Pain and disability 5 mo: I=C, 1 and 3 y: I>C Sick leave, 5 mo: not reported, 1 and 3 y: I>C‡	High
[37] Netherlands n=299	Occupational department Physician and PT	Swedish Back School including exercises (I) vs. cognitive behavioral-based back school including simulation of workplace tasks and a graded exercise program (CI) vs. usual care (Dutch guidelines) (C2)	I and C1: 2 h examination+home exercises twice daily I: 4×2 h (0.5 h education+1.5 h exercises) for 4 wk C1: 16×1 h for 8 wk	Recurrence, 3 and 6 mo: I=C1=C2 Pain: I=C1=C2 Disability, 3 mo I>C1=C2; 6 mo I=C1=C2 Sick leave (return to work): C2=I=C1 (number of sick days): I=C1=C2	High

>Significantly better than.
C=control; I=intervention; PT=physiotherapy.
* Reported.
** Invited lecturers from psychology, pedagogy, neurology, orthopedics, rehabilitation medicine, and occupational therapy.
‡ Back-related sick leave reported.

than usual care or a cognitive behavioral-based back school. We found conflicting evidence that back schools are better than waiting list, no intervention or usual care for return to work. On the basis of the included trials, we cannot recommend back schools for CLBP.

Brief education

We found strong evidence that brief education in the clinical setting is not more effective than usual care for reduction of pain and more effective than usual care for return to work. We found conflicting evidence that brief education is more effective than usual care in reducing disability. We found limited evidence that brief education provided by a back book, whether given by a health provider or distributed by e-mail, or Internet discussion is less effective than massage, yoga, and exercises, and conflicting evidence that it is more effective than waiting list for pain reduction. On the basis of the included trials, there is limited evidence that brief education is more effective than massage and no intervention, and less effective than yoga and massage for reduction of disability. There is no evidence for return to work when brief education is provided by a back book

Table 5
Brief education

Reference Country Participants	Setting Profession involved	Intervention	Duration/frequency	Effectiveness	Quality rating
[6,54] Norway n=975/489	Rehabilitation department Physiatrist, nurse, PT	Examination, information about reflex activation of spinal muscles,reassurance to reduce fear and sickness behavior, mini-back school, encourage to set their own physical activity goals (I) vs. usual care (C)	I: 1×2–3 h+1×1–2 h, reinforced after 3 mo and 1 y, open door	Pain and disability: not reported Sick leave: 1 and 5 y: I>C	High*
[55] United States n=255	Primary care Lay person with LBP	Information on red flags, common causes of LBP, factors contributing to pain, exercise, and activity, biomechanics, stress management and problem solving, book and videotapes used for self-management and exercises (I) vs. usual care (C)	I: 2 h×4 in 4 wk	Pain, 3, 6, and 12 mo: I=C Disability, 6 mo: I>C and 3 and 12 mo: I=C Sick leave: not reported	Low
[56,73] Norway n=457	Rehabilitation department Physiatrist, PT	Examination and reassurance as described by Indahl, stay active and home activity (I) vs. usual care (C)	I: 2×1–2 h	Pain and disability: not reported Sick leave: 3, 6 mo, and 3 y: I>C and at 2 y: I=C	High
[53] United States n=262	Occupational medicine, acupuncturists and massage therapists	Educational book and video (self-care) (I) vs. traditional Chinese Medical acupuncture (C1) vs. therapeutic massage (C2)	I: Self-care vs. C1 and C2: 10 visits in 10 wk	Pain (bothersomeness), 10 wk: I<C2 Disability: I=C 1>C2 Sick leave: not reported Costs: I<C2 and C2>C1	High
[58] United States n=580	Internet Physician, psychologist, PT	Back pain e-mail discussion group+a book and videotape (I) vs. subscription to a non–health-related magazine (C)	I: Not defined	Pain, 12 mo: I>C Disability: I>C Use of health care, 12 mo: I=C Sick leave: not reported	Low
[59] Norway n=93	Hospital outpatient and primary care Physiatrist, PT	Examination and reassurance as described by Indahl, assessment of function, instruction to activate deep stabilizing muscles, stay active (I) vs. examination and aerobic dance program modified for LBP patients (C1) vs. usual care (C2)	I: 2×0.5–1 h C1: 2–3×1 h weekly for 15 wk	Pain, 18 wk: I=C1=C2 Disability: I>C2 and C1=C2 Sick leave: I=C1=C2	High
[60,61] Finland n=164	Primary care, occupational medicine Physician, physiatrist, PT	Examination, information and reassurance as described by Indahl, stay active and home activity, confirmation by second physician (I) vs. same+worksite visit by physiotherapist (C1) vs. usual care (C2)	I: 2 h C1: 2+1 h	Pain and disability, 3, 6, 12, and 24 mo: I=C1=C2 Bothersomeness: I>C2=C1 Sick leave: I>C2=C1 Costs: I>C2=C1	High
[62] Sweden n=56	Recruited from newspapers Psychologist and PT	Internet-based pain management program with telephone support, discuss negative thoughts and beliefs, active coping, relaxation, stretching, exercises (I) vs. waiting list (C)	I: Active access for 8 wk	Pain, 3 mo: I=C Disability and sick leave: not reported	Low

(*Continued*)

Table 5 (*Continued*)

Reference Country Participants	Setting Profession involved	Intervention	Duration/frequency	Effectiveness	Quality rating
[48] Australia n=58	Private physiotherapy PT	I: Information based on current knowledge of neurophysiology of pain C: Information in accordance with Swedish Back School	I and C: 1×3 h+home work (questions related to the education) daily for 2 wk.	Pain: attitudes: I>C, catastrophing: I>C Disability: I>C Sick leave: not reported	High
[50] United States n=101	Nonprofit, integrated health-care system	Mailed self-care book (I*) vs. Yoga (C1) vs. exercises (information, goal-setting, aerobic, strength, and flexibility exercises) (C2)	I: Mailed back book C1 and C2: 12 weekly 75-min classes	Pain (bothersomeness), 6 wk: I<C1, 12 wk: I=C1=C2, 26 wk: I =C2<C1 Disability 6 and 26 wk: I<C1=C2, 12 wk: I=C2<C1 Sick leave: not reported	High
[52] UK n=346	Hospital—outpatient PT	Back book+back school (I) vs. spinal stabilization exercises+back school (C1) vs. manual therapy+back school (C2)	I: 3 h×1 (back school) C1 and C2: 3 h×1+ 10-wk×1 h	Pain, 6 mo: I=C2<C1 but not at 3, 12, and 24 mo Disability, 6 and 12 mo: I=C2<C1, but not at 3 and 24 mo Sick leave: not reported	Low

>Significantly better than.
PT=physiotherapy; LBP=low back pain.
* Zelens design.

or e-mail/Internet discussion. We recommend brief education in the clinical setting for return to work. We cannot recommend brief education given as a back book or Internet discussion as an alternative to other treatments.

Fear-avoidance training

We found moderate evidence that fear-avoidance training emphasizing exposure is more effective than graded activity with regard to fear avoidance, pain, and disability. On the basis of one large trial, there is limited evidence for the effectiveness with regard to pain, disability, and return to work compared with usual care. On the basis of two trials, there is limited to moderate evidence that a rehabilitation program incorporating exposure to physical activities labeled not recommended is not different from spinal fusion with regard to pain, disability, and return to work. We recommend exposure as an important element in fear-avoidance training. We recommend incorporating fear-avoidance training in a rehabilitation program as an alternative to spinal fusion.

General comments

Four of the authors were involved in at least one of the included trials. Though this may have introduced a bias in the evaluation of the studies, the authors did not evaluate a trial if they were among the authors. Blinding of the therapist and patient is impossible in all the interventions included. Thus, the observed difference between two interventions might be attributed to a specific method, positive (placebo) or negative (nocebo) expectations, or communicative skills of the therapist [70]. The latter is even considered as an essential part of the intervention. In general, differences between treatments are within the measurement error of the primary outcome variable, and the statistical significance is of doubtful clinical relevance. Often the improvements observed within both study groups are larger than the difference between the groups.

Back schools

Previous SRs included multidisciplinary interventions where the back school played a minor role. By example, in the study by Harkapaa et al. [4], patients had additionally >25 sessions of various types of therapy like exercises, massage, electrotherapy, and thermotherapy. This makes it difficult to evaluate the effectiveness of the back school. By applying more strict inclusion criteria for back schools, the homogeneity of the interventions was improved. Also, our interpretation of results in one high-quality study and one later published trial reduced the evidence for back schools that has previously been reported [3,37]. In the high-quality study, back school was significantly better only for the change between 4 and 16 weeks [3].

Brief education

Studies may have been missed by our reviews that have used brief education as the control intervention, but study selection most likely did not bias our results. Two high-quality studies reported that the addition of exercises, stabilizing exercises and manipulation, was not cost effective [7,8,47,49]. Most of the studies have been conducted in patients who are on sick leave for 8 to 12 weeks. Some of these studies have previously been classified as subacute pain, but duration refers to duration of sick leave and not of pain. Considering the delay from pain onset to sick leave and from registration by public insurance to assessment in the respective studies,

Table 6
Fear-avoidance training

Reference Country Participants	Setting Profession involved	Intervention	Duration/frequency	Effect on fear avoidance	Effectiveness	Quality rating
[63] Netherlands n=4	Experimental psychology	Exposure to fear-eliciting situations, individually tailored(I) vs. graded activity using the operant principles described by Fordyce and Lindström(C). Both treatments embedded in a comprehensive behavioral program.	3 wk	3 wk: I>C	Pain and disability, 3 wk Sick leave not reported	High*
[65] Netherlands n=6	Experimental psychology	See Vlaeyen 2001	3 wk, frequency not reported.	3 wk: I>C	Pain and disability, 3 wk Sick leave not reported	High*
[64] Netherlands n=6	Experimental psychology	Education (all) with the explanation that pain is a common condition that can be self-managed, then allocation to exposure (I) vs. graded activity (C), for details see Vlaeyen 2001.	I: 6 wk, 24 h. C: 8 wk, 32 h.	1.5 and 6 mo: I>C	Pain and disability, 1.5 and 6 mo I>C Sick leave not reported	High*
[67] USA n=240	Primary care Psychologist PT	Two visits to psychologist and PT, respectively (I) vs. treatment as usual (C).	I: 1–2 h×4 over 35 d.	2, 6, 12, 24 mo: I>C	Pain, 2, 6, 12 mo: I >C Disability, 2, 6, 12, 24 mo: I>C Sick leave,** 6, 24 mo: I>C	High
[66] Norway n=64	Hospital Physiatrist, PT, lay person	Cognitive intervention (information, reassurance, exposure) and exercises (general and stabilizing) (I) vs. instrumented lumbar fusion L4–L5 and/or L5–S1+postoperative advice by PT+exercises after 3 mo (C).	I: 1 wk at hospital+ 2 wk at home+ 2 wk at hospital	FABQ-PA, 1 y: I>C FABQ-W: I>C	Pain, disability, and sick leave, 1 y: I=C	High
[68] Norway n=60	See Brox 2003	See Brox 2003—intervention is the same, but patients with CLBP 1 y after surgery for disc herniation are included.	See Brox 2003	FABQ-PA, 1 y: I>C FABQ-W: I=C	Pain, disability, and sick leave, 1 y: I=C	High

RTW=return to work; FABQ-PA=Fear-Avoidance Beliefs Physical Activity; FABQ-W=Fear-Avoidance Beliefs Work; PT=Physiotherapist.
>Significantly more effective than.
* Crossover design.
** Includes school and housework.

the duration of pain is greater than 12 weeks and the studies therefore, include patients with CLBP.

From a theoretical point of view, there is a major difference between interventions that offer the patient a consultation including clinical examination and advice given, and a brief education consisting of a back book e-mailed to a person that might be included by advertisement. The lack of communication with a professional for the participants in a control group who receive a back book only might introduce negative expectations (nocebo) and dissatisfaction. Conversely, participation in an active group might enhance positive expectations (placebo). In at least two of the included trials, we cannot exclude that the observed negative differences are the result of placebo and nocebo effects [50,52].

One of the included studies compared neurophysiological education with the educational component of the Swedish Back School [48]. The authors reported differences in pain cognitions and physical performance, and suggested that neurophysiological—rather than back school type education—should be included in a wider pain management approach.

Fear-avoidance training

The reductions of fear-avoidance or kinesiophobic beliefs were 50% or more in the interventions emphasizing

exposure [63,65–68]. Back muscle strength and fingertip-to-floor distance were improved after cognitive intervention and exercises, supporting the link between fear avoidance and physical performance [69]. Other studies have reported that fear-avoidance beliefs are reduced after exercises and after brief education, which underline the importance of further assessment to depict the key factor for reduction of pain-related fear [48,59,71]. A study in patients with acute pain suggests that fear-avoidance training should be offered to those with high scores in fear-avoidance beliefs [72].

CBT interventions in CLBP may not adequately address and reduce pain-related fear [37]. The trial suggested that a comprehensive CBT intervention in patients with moderate complaints was less effective than a brief education type back school in reducing kinesiophobia.

Studies to compare the cost effectiveness of brief education by a physician or a physiotherapist (or both) or with a back school are warranted. More studies are recommended to evaluate fear-avoidance training as part of usual care and to better understand indications, content, and number of sessions needed.

On the basis of the included trials, we cannot recommend back schools, but consistent positive results in one high-quality study warrant more research. We recommend brief education for reduction of sick leave. Back book or Internet discussions cannot be recommended as an alternative to other treatments. We recommend fear-avoidance training incorporated in a rehabilitation program as an alternative to spinal fusion, but more research is warranted to clarify indications and components of the intervention.

References

[1] Zachrisson-Forssell M. The Swedish back school. Physiotherapy 1980;66:112–4.

[2] Nachemson A, Elfstrom G. Intravital dynamic pressure measurements in lumbar discs. A study of common movements, maneuvers and exercises. Scand J Rehabil Med Suppl 1970;1:1–40.

[3] Klaber Moffett JA, Chase SM, Portek I, Ennis JR. A controlled, prospective study to evaluate the effectiveness of a back school in the relief of chronic low back pain. Spine 1986;11:120–2.

[4] Harkapaa K, Jarvikoski A, Mellin G, Hurri H. A controlled study on the outcome of inpatient and outpatient treatment of low back pain. Part I. Pain, disability, compliance, and reported treatment benefits three months after treatment. Scand J Rehabil Med 1989;21:81–9.

[5] Waddell G. 1987 Volvo award in clinical sciences. A new clinical model for the treatment of low-back pain. Spine 1987;12:632–44.

[6] Indahl A, Velund L, Reikeraas O. Good prognosis for low back pain when left untampered. A randomized clinical trial. Spine 1995;20:473–7.

[7] Frost H, Lamb SE, Doll HA, Carver PT, Stewart-Brown S. Randomised controlled trial of physiotherapy compared with advice for low back pain. BMJ 2004;329:708.

[8] Rivero-Arias O, Gray A, Frost H, Lamb SE, Stewart-Brown S. Cost-utility analysis of physiotherapy treatment compared with physiotherapy advice in low back pain. Spine 2006;31:1381–7.

[9] Cherkin DC, Deyo RA, Street JH, Hunt M, Barlow W. Pitfalls of patient education. Limited success of a program for back pain in primary care. Spine 1996;21:345–55.

[10] Lethem J, Slade PD, Troup JD, Bentley G. Outline of a Fear-Avoidance Model of exaggerated pain perception—I. Behav Res Ther 1983;21:401–8.

[11] Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain 1993;52:157–68.

[12] Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain 2000;85:317–32.

[13] Keller A, Johansen JG, Hellesnes J, Brox JI. Predictors of isokinetic back muscle strength in patients with low back pain. Spine 1999;24:275–80.

[14] Brox JI, Brevik JI, Ljunggren AE, Staff PH. Influence of anthropometric and psychological variables pain and disability on isometric endurance of shoulder abduction in patients with rotator tendinosis of the shoulder. Scand J Rehabil Med 1996;28:193–200.

[15] Vlaeyen JW, Kole-Snijders AM, Boeren RG, van EH. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. Pain 1995;62:363–72.

[16] Al-Obaidi SM, Nelson RM, Al-Awadhi S, Al-Shuwaie N. The role of anticipation and fear of pain in the persistence of avoidance behavior in patients with chronic low back pain. Spine 2000;25:1126–31.

[17] Moseley GL. Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain. Eur J Pain 2004;8:39–45.

[18] Crombez G, Vlaeyen JW, Heuts PH, Lysens R. Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. Pain 1999;80:329–39.

[19] Airaksinen O, Brox JI, Cedraschi C, et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. Eur Spine J 2006;15:S192–300.

[20] Kori SH, Miller RP, Todd DD. Kinesiophobia: a new view of chronic pain behavior. Pain Manag 1990;3:35–43.

[21] Grotle M, Vollestad NK, Veierod MB, Brox JI. Fear-avoidance beliefs and distress in relation to disability in acute and chronic low back pain. Pain 2004;112:343–52.

[22] Ursin H. Press stop to start: the role of inhibition for choice and health. Psychoneuroendocrinology 2005;30:1059–65.

[23] Eriksen HR, Murison R, Pensgaard AM, Ursin H. Cognitive activation theory of stress (CATS): from fish brains to the Olympics. Psychoneuroendocrinology 2005;30:933–8.

[24] Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. J Clin Epidemiol 1991;44:1271–8.

[25] van Tulder MW, Assendelft WJ, Koes BW, Bouter LM. Method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group for Spinal Disorders. Spine 1997;22:2323–30.

[26] Heymans MW, van Tulder MW, Esmail R, Bombardier C, Koes BW. Back schools for nonspecific low back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine 2005;30:2153–63.

[27] Cohen JE, Goel V, Frank JW, Bombardier C, Peloso P, Guillemin F. Group education interventions for people with low back pain. An overview of the literature. Spine 1994;19:1214–22.

[28] Koes BW, van Tulder MW, van der Windt WM, Bouter LM. The efficacy of back schools: a review of randomized clinical trials. J Clin Epidemiol 1994;47:851–62.

[29] van Tulder MW, Esmail R, Bombardier C, Koes BW. Back schools for non-specific low back pain. Cochrane Database Syst Rev 2000;CD000261.

[30] Maier-Riehle B, Harter M. The effects of back schools—a meta-analysis. Int J Rehabil Res 2001;24:199–206.

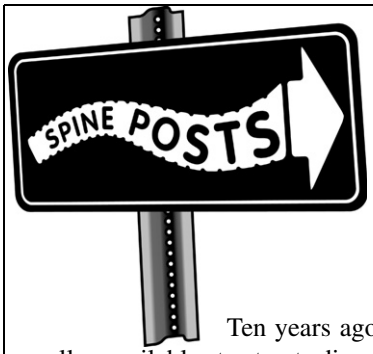
[31] Tveito TH, Hysing M, Eriksen HR. Low back pain interventions at the workplace: a systematic literature review. Occup Med (Lond) 2004;54:3–13.

[32] Kool JP, Oesch PR, Bachmann S, et al. Increasing days at work using function-centered rehabilitation in nonacute nonspecific low back pain: a randomized controlled trial. Arch Phys Med Rehabil 2005;86:857–64.
[33] Linton SJ, Bradley LA, Jensen I, Spangfort E, Sundell L. The secondary prevention of low back pain: a controlled study with follow-up. Pain 1989;36:197–207.
[34] Penttinen J, Nevala-Puranen N, Airaksinen O, Jaaskelainen M, Sintonen H, Takala J. Randomized controlled trial of back school with and without peer support. J Occup Rehabil 2002;12: 21–9.
[35] Postacchini F, Facchini M, Palieri P. Efficacy of various forms of conservative treatment in low back pain: a comparative study. Neuroorthopedics 1988;6:28–35.
[36] Dalichau S, Perrey RM, Solbach T, Elliehausen HJ. Erfahrungen bei der Durchfuhrung eines berufsbezogenen Rückenschulmodells in Baugewerbe. Arbeitsmedizin 1998;48:72–80.
[37] Heymans MW, de Vet HC, Bongers PM, Knol DL, Koes BW, van MW. The effectiveness of high-intensity versus low-intensity back schools in an occupational setting: a pragmatic randomized controlled trial. Spine 2006;31:1075–82.
[38] Lankhorst GJ, Van de Stadt RJ, Vogelaar TW, Van der Korst JK, Prevo AJ. The effect of the Swedish Back School in chronic idiopathic low back pain. A prospective controlled study. Scand J Rehabil Med 1983;15:141–5.
[39] Hurri H. The Swedish back school in chronic low back pain. Part I. Benefits Scand J Rehabil Med 1989;21:33–40.
[40] Keijsers JF, Groenman NH, Gerards FM, van OE, Steenbakkers M. A back school in The Netherlands: evaluating the results. Patient Educ Couns 1989;14:31–44.
[41] Keijsers J, Steenbakkers M, Meertens RM, Bouter LM, Kok GJ. The efficacy of the back school: a randomized trial. Arthritis Care Res 1990;3:204–9.
[42] Donchin M, Woolf O, Kaplan L, Floman Y. Secondary prevention of low-back pain. A clinical trial. Spine 1990;15:1317–20.
[43] Lonn JH, Glomsrod B, Soukup MG, Bo K, Larsen S. Active back school: prophylactic management for low back pain. A randomized, controlled, 1-year follow-up study. Spine 1999;24:865–71.
[44] Glomsrod B, Lonn JH, Soukup MG, Bo K, Larsen S. ''Active back school'', prophylactic management for low back pain: three-year follow-up of a randomized, controlled trial. J Rehabil Med 2001;33: 26–30.
[45] Hay EM, Mullis R, Lewis M, et al. Comparison of physical treatments versus a brief pain-management programme for back pain in primary care: a randomised clinical trial in physiotherapy practice. Lancet 2005;365:2024–30.
[46] Moseley L. Combined physiotherapy and education is efficacious for chronic low back pain. Aust J Physiother 2002;48:297–302.
[47] Niemisto L, Lahtinen-Suopanki T, Rissanen P, Lindgren KA, Sarna S, Hurri H. A randomized trial of combined manipulation, stabilizing exercises, and physician consultation compared to physician consultation alone for chronic low back pain. Spine 2003;28: 2185–91.
[48] Moseley GL, Nicholas MK, Hodges PW. A randomized controlled trial of intensive neurophysiology education in chronic low back pain. Clin J Pain 2004;20:324–30.
[49] Niemisto L, Rissanen P, Sarna S, Lahtinen-Suopanki T, Lindgren KA, Hurri H. Cost-effectiveness of combined manipulation, stabilizing exercises, and physician consultation compared to physician consultation alone for chronic low back pain: a prospective randomized trial with 2-year follow-up. Spine 2005;30:1109–15.
[50] Sherman KJ, Cherkin DC, Erro J, Miglioretti DL, Deyo RA. Comparing yoga, exercise, and a self-care book for chronic low back pain: a randomized, controlled trial. Ann Intern Med 2005;143: 849–56.
[51] Williams KA, Petronis J, Smith D, et al. Effect of Iyengar yoga therapy for chronic low back pain. Pain 2005;115:107–17.
[52] Goldby LJ, Moore AP, Doust J, Trew ME. A randomized controlled trial investigating the efficiency of musculoskeletal physiotherapy on chronic low back disorder. Spine 2006;31:1083–93.
[53] Cherkin DC, Eisenberg D, Sherman KJ, et al. Randomized trial comparing traditional Chinese medical acupuncture, therapeutic massage, and self-care education for chronic low back pain. Arch Intern Med 2001;161:1081–8.
[54] Indahl A, Haldorsen EH, Holm S, Reikeras O, Ursin H. Five-year follow-up study of a controlled clinical trial using light mobilization and an informative approach to low back pain. Spine 1998;23: 2625–30.
[55] Von KM, Moore JE, Lorig K, et al. A randomized trial of a lay person-led self-management group intervention for back pain patients in primary care. Spine 1998;23:2608–15.
[56] Hagen EM, Eriksen HR, Ursin H. Does early intervention with a light mobilization program reduce long-term sick leave for low back pain? Spine 2000;25:1973–6.
[57] Hagen HEM, Grasdal A, Eriksen HR. Does early intervention with a light mobilization program reduce long-term sick leave for low back pain: a 3-year follow-up study. Spine 2003;28:2309–15.
[58] Lorig KR, Laurent DD, Deyo RA, Marnell ME, Minor MA, Ritter PL. Can a Back Pain E-mail Discussion Group improve health status and lower health care costs?: a randomized study. Arch Intern Med 2002;162:792–6.
[59] Storheim K, Brox JI, Holm I, Koller AK, Bo K. Intensive group training versus cognitive intervention in sub-acute low back pain: short-term results of a single-blind randomized controlled trial. J Rehabil Med 2003;35:132–40.
[60] Karjalainen K, Malmivaara A, Pohjolainen T, et al. Mini-intervention for subacute low back pain: a randomized controlled trial. Spine 2003;28:533–40.
[61] Karjalainen K, Malmivaara A, Mutanen P, Roine R, Hurri H, Pohjolainen T. Mini-intervention for subacute low back pain: two-year follow-up and modifiers of effectiveness. Spine 2004;29: 1069–76.
[62] Buhrman M, Faltenhag S, Strom L, Andersson G. Controlled trial of Internet-based treatment with telephone support for chronic back pain. Pain 2004;111:368–77.
[63] Vlaeyen JW, de Jonge J, Geilen M, Heuts PH, van BG. Graded exposure in vivo in the treatment of pain-related fear: a replicated single-case experimental design in four patients with chronic low back pain. Behav Res Ther 2001;39:151–66.
[64] de J Jr, Vlaeyen JW, Onghena P, Goossens ME, Geilen M, Mulder H. Fear of movement/(re)injury in chronic low back pain: education or exposure in vivo as mediator to fear reduction? Clin J Pain 2005;21:9–17.
[65] Vlaeyen JW, de Jonge J, Geilen M, Heuts PH, van BG. The treatment of fear of movement/(re)injury in chronic low back pain: further evidence on the effectiveness of exposure in vivo. Clin J Pain 2002;18: 251–61.
[66] Brox JI, Sorensen R, Friis A, et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. Spine 2003;28:1913–21.
[67] Von Korff M, Balderson BH, Saunders K, et al. A trial of an activating intervention for chronic back pain in primary care and physical therapy settings. Pain 2005;113:323–30.
[68] Brox JI, Reikeras O, Nygaard O, et al. Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous surgery for disc herniation: a prospective randomized controlled study. Pain 2006;122:145–55.
[69] Keller A, Brox JI, Gunderson R, Holm I, Friis A, Reikeras O. Trunk muscle strength, cross-sectional area, and density in patients with chronic low back pain randomized to lumbar fusion or cognitive intervention and exercises. Spine 2004;29:3–8.
[70] Thompson GW. The placebo effect and health. New York: Prometheus Books, 2005.

[71] Mannion AF, Muntener M, Taimela S, Dvorak J. A randomized clinical trial of three active therapies for chronic low back pain. Spine 1999;24:2435–48.

[72] George SZ, Fritz JM, Bialosky JE, Donald DA. The effect of a fear-avoidance-based physical therapy intervention for patients with acute low back pain: results of a randomized clinical trial. Spine 2003;28: 2551–60.

[73] Hagen KB, Hilde G, Jamtvedt G, Winnem M. Bed rest for acute low-back pain and sciatica. Cochrane Database Syst Rev 2004; CD001254.



10 Years Ago in Spine

Ten years ago, no approach was clinically available to treat disc degeneration. The disc seemed to have only limited ability to repair itself because of the difficulty in sustaining the delivery of growth factor proteins to patients, especially those with chronic conditions.

However, advances at that time revealed the potential use of gene therapy not only for classic genetic disorders but also for acquired diseases, including disorders of the musculoskeletal system. Thus, an alternative therapy to the use of growth factors for disc regeneration was the use of gene transfer to genetically modify the disc cells so that the cells continuously manufactured the desired growth factors themselves. Successful gene therapy depended not only on efficient gene transfer to the cells, but also on the expression of transgenes for sufficiently long periods.

Up to that point, successful transfer of exogenous genes to the intervertebral disc in vivo had not been reported. In this study, the authors investigated the possible use of gene therapy in rabbits for treating various disorders of the intervertebral disc and studied the feasibility of direct gene transfer to the intervertebral disc. Specifically, the authors sought to determine whether it was possible to transfer genes to cells within the intervertebral disc by direct injection of an adenovirus, and examined the duration of gene expression obtained by this method.

Because of the intervertebral disc's uniquely low oxygen tension, poor nutrition, and acidic pH, the authors determined that in vivo methods (in which the vectors with the appropriate genes are introduced directly into the body) offered greater advantages than ex vivo methods (in which the target cells are removed, cultured, genetically altered in vitro, and then reimplanted) for gene delivery.

The adenovirus vector was selected for the in situ infection of nucleus pulposus cells because of its availability in high titers and its ability to diffuse through the matrix of the nucleus pulposus and infect nondividing, highly differentiated cells. The in vitro component of the study used four rabbits in evaluating nucleus pulposus cell culture and transduction in vitro. The in vivo component used 15 other rabbits in the evaluation of transduction in vivo and Lac-Z marker gene expression.

The authors reported that exogenous genes were successfully delivered to cells within the intervertebral disc in vitro and in vivo by means of a direct adenovirus-mediated gene transfer technique [1]. A high rate of gene transfer into nucleus pulposus cells was observed, followed by prolonged transgene expression in vivo (3 months). These results showed the feasibility of adenovirus-mediated gene transfer to the intervertebral disc.

This successful demonstration of adenovirus-mediated exogenous gene transfer to the disc and of sustained, long-term expression suggested that the adenoviral vector was suitable for delivery of appropriate genes to the disc for the treatment of spinal disorders, and that adenovirus-mediated gene transfer had the potential to open a new avenue for the treatment of intervertebral disc disorders. None of the rabbits showed any evidence of systemic disease.

The authors hypothesized that the relatively encapsulated and avascular environment of the nucleus pulposus limited the access of immunocompetent cells, thereby preventing immune reactivity and prolonging gene expression. The authors recommended further studies to investigate: 1) the use of adenovirus-mediated in vivo gene therapy for disorders of the intervertebral disc; 2) the maximum length of expression of the transgene; and 3) whether there is a delayed immune response to the viral antigen and late toxic effects to the target cells.

Reference

[1] Nishida K, Kang JD, Suh J, Robbins PD, Evans CH, Gilbertson LG. Adenovirus-mediated gene transfer to nucleus pulposus cells: implications for the treatment of intervertebral disc degeneration. Spine 1998;23:2437–42.