COURSE AND PROGNOSIS

Karin Verkerk

Chronic Non-Specific Low Back Pain

Course and prognosis

Spine & Joint Centre
samen in beweging

Chronic Non-Specific Low Back Pain

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Karin Verkerk

Hogeschool Rotterdam Uitgeverij

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Course and prognosis

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Beloop en prognose

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CHAPTER 1

General introduction

Chronic non-specific back pain

In the Netherlands, the annual incidence of back pain in the general population is estimated at 10-15%.[1] In Canada, the annual (cumulative) incidence of low back pain in the general population is 18.6%.[2] In 1999, in the Netherlands, chronic non-specific low back pain was reported by 16.0% of working men, by 23.1% of non-working men, by 17.9% of working women and by 27.4% of non-working women.[3] In 2009, 33.2 per 1,000 patients Registered in general practice contacted the general practitioner (GP) because of low back pain.[4] On average, these patients had contact with their GP two times in the form of a consultation (42.4%). Of these patients, over 15% were referred to another healthcare discipline, mainly to a physiotherapist (63.8%).[4]

The clinical guidelines recommend to focus on identification of 'red flags' to determine whether the patient is suffering from non-specific back pain or whether there is a suspicion of serious pathology.[5,6] The GP and physiotherapist are advised to initially treat patients with non-specific back pain in a conservative way, which includes informing the patient about the expected course, prescription of (pain) medication (by the GP) and the general recommendation that the patient should remain as active as possible.[5,6] After 12 weeks, low back pain is labelled as chronic non-specific low back pain and the Dutch GP Guideline[6] recommends to consider cognitive behavioural therapy; this is because it is increasingly likely that psychological factors (e.g. fear of movement, illness perception) and/or the workplace, play a role. In this case, referral by a GP to multidisciplinary treatment is then advised. If there is suspicion of a specific (physical) cause, this should first be excluded by an orthopaedic surgeon, neurologist or rheumatologist, before the patient is referred to a multidisciplinary centre.[6]

In this thesis, chronic 'non-specific low back pain' is defined as low back pain without a specific physical cause, such as nerve root compression (the radicular syndrome), trauma, infection, or the presence of a tumour.

Pain in the lumbosacral region is the most common symptom in patients with non-specific low back pain. Pain may also radiate to the gluteal region to the thighs, or to both. The duration of this type of back pain is defined as lasting longer than 3 months.[5]

Course of (chronic) non-specific back pain

The term 'course' can refer to both the natural and the clinical course of low back pain.[7] The natural course (in contrast to the clinical course) refers to the 'normal' course of low back pain without any intervention. We expect that the natural and clinical course will differ for each phase, starting with acute (< 12 weeks) and progressing to chronic (> 12 weeks) non-specific low back. We also expect different prognostic factors for the natural and clinical course of non-specific low back pain.[8] A systematic review on the prognosis and long-term course of low back pain indicates that, after an episode of low back pain, 44% to 78% of the patients suffer from a relapse of back pain, and that 26% to 37% suffer from recurrent sick leave.[9]

Furthermore, after 3 months the pain and disability level decrease, although disability tends to persist for at least 12 months or patients will have at least one recurrence within 12 months.[7] Cassidy et al. describe similar results, indicating that low back pain is a common, chronic and recurrent condition in the general population.[2] Younger people are less likely to have persistent low back pain and more likely to have complete resolution of symptoms.[2] A recent meta-analysis confirms earlier findings describing the course for patients with acute (< 12 weeks) or persistent (> 12 weeks to 12 months) low-back pain for the outcome pain, disability, or recovery.[10]

After an intervention, both acute and persistent low back pain improve in the first 6 weeks and, thereafter, improvement slows down. Low to moderate levels of pain and disability may still be present at 12 months, especially in cohorts with persistent pain. Other studies show that the course can differ per patient or group: some improve more rapidly, some more slowly, whereas others may fluctuate.[11] This difference might be explained by the inclusion of different study populations and/or the use of different outcomes to define recovery.[8,10,11]

Prognosis of (chronic) non-specific back pain

Chronic non-specific low back pain is assumed to be a multi-factorial affliction, implying that a number of different risk factors contribute to its development and persistence.[8,10,12,13] After onset, prognostic factors can potentially predict the future course.

Risk factors for the development of chronic pain (i.e. transition from acute to chronic pain) are well documented in the literature.[8,12,14,15] However, when pain becomes persistent, less knowledge is available on the risk factors for future outcome. Increased knowledge on the prognostic factors for chronic complaints will allow to better inform and advise patients, by supporting clinical decisions about the type of treatment and identifying patients at risk of a poor outcome.[8,14] A study from Australia reported that the prognosis is less favourable for those who: a) have taken previous sick leave for low back pain, b) have more disability or severe pain intensity at onset of chronic non-specific low back pain, c) have a lower education level, d) perceive themselves as having a high risk of persistent pain, and e) were born outside Australia.[12]

Outcome of (chronic) non-specific back pain

The objective of this thesis is to describe the clinical course of chronic non-specific low back pain in patients referred to a rehabilitation centre in tertiary care, to identify prognostic factors for recovery, and to analyse the influence of various outcomes and statistical techniques on the development of a prognostic model. We used outcome measures that are similar to those utilised since 2000, when an international panel of experts on low back pain agreed on a core set of outcome measures. This core set includes five domains: 1) low back pain intensity, 2) low-back-pain-specific disability, 3) return to work, 4) generic functional status, and 5) patient's satisfaction with the process of care and treatment outcome.[16]

Ostelo et al. stated that, when measuring outcomes in patients, there is no consensus in the literature on the most appropriate technique to use to determine the 'minimal clinically important change' (MCIC).[17,18] Two adequate and frequently used methods to estimate the MCIC are the smallest change possible to detect improvement (between baseline and follow-up) and to estimate the optimal cut-off point. For example, the Quebec Back Pain Disability Scale (QBPDS; range 0-100) was dichotomised into "no improvement in disability" and "improvement in disability," using a reduction of 30% at follow-up compared to baseline as a clinically relevant difference[17-19] and 'absolute recovery' was defined as a QBPDS score of ≤ 20 points at follow-up.[13,17,20,21] Ostelo et al. reported that the change from baseline to follow-up can be defined as 'clinically important' (e.g. a 30% improvement) because individual patients determine their own health status.[17] For each outcome, except for generic functional status, an indicator is suggested to determine the MCIC between baseline and follow-up.[17,18,20-22] However, an ongoing discussion is whether the MCIC is better expressed as a percentage of improvement (e.g., > 30% improvement on the scale) or as a cut-off point (dichotomisation) in order to determine recovery.[17,18,20-22]

In our study, recovery as assessed with various outcome measures was operationalised according to two definitions: 1) a 30% improvement compared to baseline scores with regard to the outcomes back pain intensity, disability, work participation and quality of life (SF-36; 10% improvement)[17-19] and 2) 'absolute recovery' was defined with a Visual Analogue Scale score of pain intensity ≤ 10 mm, disability with the QBPDS score of ≤ 20 points, work participation (0-100% working) ≥ 90% at follow-up, and global perceived effect (GPE) on a 5-point scale dichotomised into 'clinically improved' vs. 'clinically not improved'.[13,17,20,21,23]

Multidisciplinary treatment in the Spine & Joint Centre

Management of chronic non-specific low back pain in the sense of treatment after a lack of successful recovery in primary care (e.g. GP, physiotherapist) consists of behavioural treatment and/or multidisciplinary rehabilitation.[5,6,24,25] A systematic review showed moderate quality of evidence that, for pain relief on the short-term, operant therapy is more effective than a waiting list and that behaviour therapy is more effective than usual care.[25] However, no specific type of behaviour therapy has been shown to be more effective than another. On the long term, there appears to be little difference between behaviour therapy and group exercises for pain or depressive symptoms.[25]

Another systematic review using the same core set of outcomes as used in this thesis, reported moderate evidence that intensive multidisciplinary bio-psychosocial rehabilitation with functional restoration is more effective in reducing pain compared with outpatient nonmultidisciplinary rehabilitation or usual care.[24]

There is contradictory evidence regarding vocational outcomes of an intensive multidisciplinary bio-psychosocial intervention. Some trials report improvements in work readiness, whereas others shows no significant reduction in sick leave. Less intensive outpatient psychophysical treatments did not improve pain, function or vocational outcomes when compared with nonmultidisciplinary outpatient therapy or usual care. Few trials have reported on the effects on quality of life or global assessments.[24]

In the cohort study presented in this thesis, all patients received multidisciplinary treatment at the Spine & Joint Centre (Rotterdam) using a bio-psychosocial approach to stimulate patients to adopt adequate (movement) behaviour aimed at physical and functional recovery. The therapy program consisted of 16 sessions of 3 hours each during a 2-month period (a total of 48 hours), coached by a multidisciplinary team (physical therapist, physician, health scientist, psychologist). Behavioural principles were applied to encourage patients to adopt adequate normal behavioural movement aimed at physical recovery.

Five months after the start of the therapy program (2 months twice a week at the rehabilitation centre + 3 months self-supporting activity) the patients were measured again. At 12 months the follow-up measurement was performed by postal questionnaires sent to all participating patients.

Aim of thesis

This thesis was conducted to describe and gain insight into: 1) the characteristics and clinical course of patients with non-specific low back pain treated in a tertiary rehabilitation centre, and 2) the prognostic factors for recovery (including internal validation) of patients with chronic non-specific low back pain treated in a tertiary rehabilitation centre.

Content of the thesis

Chapter 2 presents the results of a systematic review on the prognostic factors for recovery in chronic non-specific low back pain.
Chapter 3 describes the study design, the multidisciplinary treatment at the Spine & Joint Centre, and the baseline characteristics of patients in the prospective cohort study on chronic non-specific low back pain.
Chapter 4 presents the 2-, 5- and 12-months course of back pain intensity and the identified prognostic factors for the outcome 'back pain intensity' at 5- and 12-months follow-up.
Chapter 5 presents the 2-, 5- and 12-months course of back pain disability and the identified prognostic factors for the outcome 'back pain disability' at 5- and 12-months follow-up.
Chapter 6 reports the 5- and 12-months course of work participation and the identified prognostic factors for the outcome 'work participation' at 5- and 12-months follow-up.
Chapter 7 describes the 2-, 5- and 12-months course of quality of life and global perceived effect, and the identified prognostic factors for the outcomes 'quality of life' and 'global perceived effect' at 5- and 12-months follow-up.
Chapter 8 addresses the main results of this thesis, discusses implications for daily practice, and makes some recommendations for further research.

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CHAPTER 2

Prognostic factors for recovery in chronic non-specific low back pain: a systematic review

Verkerk K., Luijsterburg P.A.J., Miedema H.S., Pool-Goudzwaard A.L., Koes B.W.

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Abstract

Background. Few data are available on predictors for a favorable outcome in patients with chronic non-specific low back pain (CNLBP).
Purpose. The aim of this study was to assess prognostic factors for pain intensity, disability, return to work, quality of life, or global perceived effect in patients with CNLBP at short-term (≤ 6 months) and long-term (> 6 months) follow-up.
Data Sources. Relevant studies evaluating the prognosis of CNLBP were searched in PubMed, CINAHL and EMBASE (through March 2010).
Study Selection. Articles with all types of study design were included. Inclusion criteria were: participants were patients suffering from CNLBP (≥12 weeks' duration), participants were older than 18 years of age; and the study was related to prognostic factors for recovery. Fourteen studies met the inclusion criteria.
Data Extraction. Two reviewers extracted the data and details of each study.
Data Synthesis. A qualitative analysis using ''level of evidence'' was performed for all included studies. Data was summarized in tables and critically appraised.
Limitations. The results of the studies reviewed were limited by their methodological weaknesses.

Conclusion. At short-term follow-up, no association was found for the factors age and sex with the outcomes of pain intensity and disability. At long-term follow-up, smoking had the same result. At long-term follow-up, pain intensity and fear of movement had no association with disability. At short-term follow-up, conflicting evidence was found for the association between the outcomes pain intensity and disability and the factor fear of movement. At long-term follow-up, conflicting evidence was found for the factors age, sex and physical job demands. At long-term follow-up, conflicting evidence was also found for the association between return to work and age, sex and activities of daily living. At baseline, there was limited evidence of a positive influence of lower pain intensity and physical job demands on return to work. No high-quality studies were found for the outcomes quality of life and global perceived effect.

Keywords: chronic low back pain; prognosis; systematic review

Introduction

Prognostic factors are important in providing clinicians information related to clinical decision-making, understanding of the disease process, defining the risk groups based on prognosis, and allowing more accurate prediction of disease outcome.[1] Prognostic factors are suspected to differ between acute nonspecific low back pain (NLBP) and chronic nonspecific low back pain (CNLBP) because the natural course of these 2 conditions also differs.[2]

Some data are available (based on systematic reviews) on prognostic factors from acute NLBP and the transition from acute to CNLBP, but not for the course of CNLBP.[3-8] Given its high rate of prevalence, investigation of the course of CNLBP and possible prognostic factors is needed for effective patient management, especially when modifiable prognostic factors can be identified. However, little information is available about CNLBP. One review found consistent evidence that in patients with CNLBP, expectations regarding recovery were a predictor for the decision to return to work.[9]

There is growing interest in the course and prognostic factors of CNLBP and in the various outcomes related to the recovery of patients with CNLBP.[6,10]

The aim of this systematic review was to determine prognostic factors for the outcomes pain intensity, disability, return to work, quality of life, and global perceived effect in patients with CNLBP at short-term and long-term follow-ups.

Materials and Method

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA statement) was used for this systematic review.[11]

Data sources and searches

Using the strategy of broad search terms for systematic reviews on prognostic research,[12] one reviewer (K.V.) searched for eligible studies in PubMed/MEDLINE (1966 through March 2010), CINAHL (1984 through March 2010), EMBASE (1950 through March 2010), Cochrane Library (Cochrane Central Register of Reviews and Trials through March 2010) and PEDro (1929 through March 2010). Appendix 1 shows the full search strategy with the key words used (MeSH, EMTREE and text words). Full-text articles published in English, Danish, Norwegian, Swedish and Dutch were eligible. The inclusion criteria for this review were applied independently by 2 reviewers (K.V., P.A.J.L.). First, they screened the title, key words and abstract for eligibility. Secondly, they assessed the selected full-text papers with regard to the inclusion criteria (i.e., design, participants, and reported outcomes and prognostic factors). In case of disagreements, the consensus method was used to discuss and resolve disagreement. When disagreement persisted a third independent reviewer (B.W.K.) was consulted for a final decision. The reference lists of all full-text articles were checked for eligibility.

Study selection

Only randomized cohorts designs, including randomised controlled trials that reported regarding prognostic factors on targeted outcomes, were eligible. The studies had to meet the following criteria: (1) the focus was on patients with CNLBP (≥ 12 weeks' duration), defined as low back pain that has no specified physical cause (e.g., nerve root compression, trauma, infection or the presence of a tumor), and (2) participants were older than 18 years of age. Pain in the lumbosacral region is the most common symptom in patients with NLBP. Pain may radiate to the gluteal region or to the thighs, and/or to both.[13]

A study was excluded when the study population had a specific pathology (e.g., lumbar radicular syndrome, oncological disease, arthritis, rheumatoid arthritis, systemic impairments, fractures, dislocation of the lumbar or sacral spine) or the primary aim of the study was to identify etiological factors.

Outcomes of interest were: (1) pain intensity, (2) disability, (3) return to work, (4) quality of life, and (5) global perceived effect. All reported prognostic factors (measured at baseline) on these outcomes at short-term (≤ 6 months) and long-term (> 6 months) follow-up were reviewed.

Data extraction and quality assessment

Two reviewer (K.V., P.A.J.L.) extracted data on study population, design, setting, follow-up period, loss to follow-up, prognostic factors, outcomes, and strength of association using a standardized form. The associations at short-term and long-term follow-up (reported by odds ratios or relative risk values, with corresponding *P* value or 95% confidence interval) between the prognostic factors and the outcomes were extracted or calculated by the reviewers.

The methodological quality of the studies was assessed using the Quality In Prognosis Studies (QUIPS) with a list of issues or considerations.[4,12,14] Detailed information about the issues or considerations can be retrieved by the first author. We adjusted the criteria list aimed at our population, establishing criteria for follow-up en dropout percentage[15,16] and scoring each item with ''yes'', ''no'', or ''don't know'', which led to the overall scoring of low, moderate or high risk of bias per domain.

The quality assessment considered 6 domains of potential biases: (1) study participation, (2) study attrition, (3) measurement of prognostic factors, (4) measurement of and controlling for confounding variables, (5) measurement of outcomes, and (6) analysis approaches (Appendix 2).[14] All criteria were first scored as follows: ''yes'' (Y) for informative description of the criterion at issue and study meets the criterion; ''no'' (N) for informative description, study does not meet the criterion, or there is no information; or ''don't know'' (U) for information that is lacking or insufficient. The issues were not rated or scored individually, but taken together to create an overall judgement for each of the domains of potential bias. For each of the 6 potential biases, a study was rated as having low, moderate or high risk of bias per domain. All criteria were weighted equally. We considered a study to be of high quality when the methodological risk of bias score was rated with low or moderate risk on all of the 6 important domains.

Two reviewers independently assessed the methodological quality of the included studies. Discrepancies were resolved by discussion until consensus was reached. The reviewers were not blinded to the authors or the journal name. The interobserver agreement of the quality assessment and data extraction was calculated using percentage agreement.

Data synthesis and analysis

Because of the many different potential prognostic factors that were presented actors in the included studies, the methodological heterogeneity, and the low response rate (one author responded, but incorrectly), we refrained from statistical pooling.

The strength of evidence for the reported prognostic factors associated with recovery for the outcomes pain intensity, disability, return to work, quality of life, and global perceived effect was assessed by 4 levels of evidence[17]: (1) consistent evidence: consistent findings in 2 or more studies or at least 75% of the studies

reporting similar conclusions (1 of the studies should be of high quality); (2) limited evidence: findings in 1 study of high quality or 2 or more of low quality; (3) conflicting evidence: < 75% of available studies reported similar findings, or contradictory findings present within 1 study; and (4) no evidence: no associations with an outcome of interest.[9]

Results

Search strategy and selection criteria

The search identified 6,755 citations (Figure 1). In the first round, 2 reviewers (K.V., P.A.J.L.) included 123 studies. Finally, 14 studies met all inclusion criteria and were included in the review.[18-31]

Study characteristics

Table 1 presents the characteristics of the included studies.

Design of the studies

Of the 14 included studies, 8 were prospective cohort studies[18,23,24,26-29,31] and 3 were randomised controlled trials.[20,25,30] Of 3 the remaining studies, 1 was a prospective case series[21], 1 was a retrospective correlation study,[22] and the 1 a retrospective case series.[19]

The follow-up period ranged from 6 weeks[22] to 4 years.[29] The percentage loss to follow-up ranged from 0% to 23%[18-20,24,26-31] or was unclear.[21-23,25]

Study population

Seven studies[19-21, 24, 28, 30, 31] included patients from either rehabilitation or specialized back centers, 2 included patients from an orthopedic outpatient clinic,[25,27] and 4 included patients from other rehabilitations settings such as a primary care clinic[23], hospital,[22] or general practice.[29] The setting of recruitment was not specified by Hanson and Hanson[26] and Anema et al.,[18] both reporting on the same multinational study.

Sample size ranged from 50[24] to 5,035[29] patients, with 10 studies enrolling more than 100 patients. Mean age of the patients ranged from 36 to 46 years, and the male-female ratio ranged from 10:1 to 1:1.

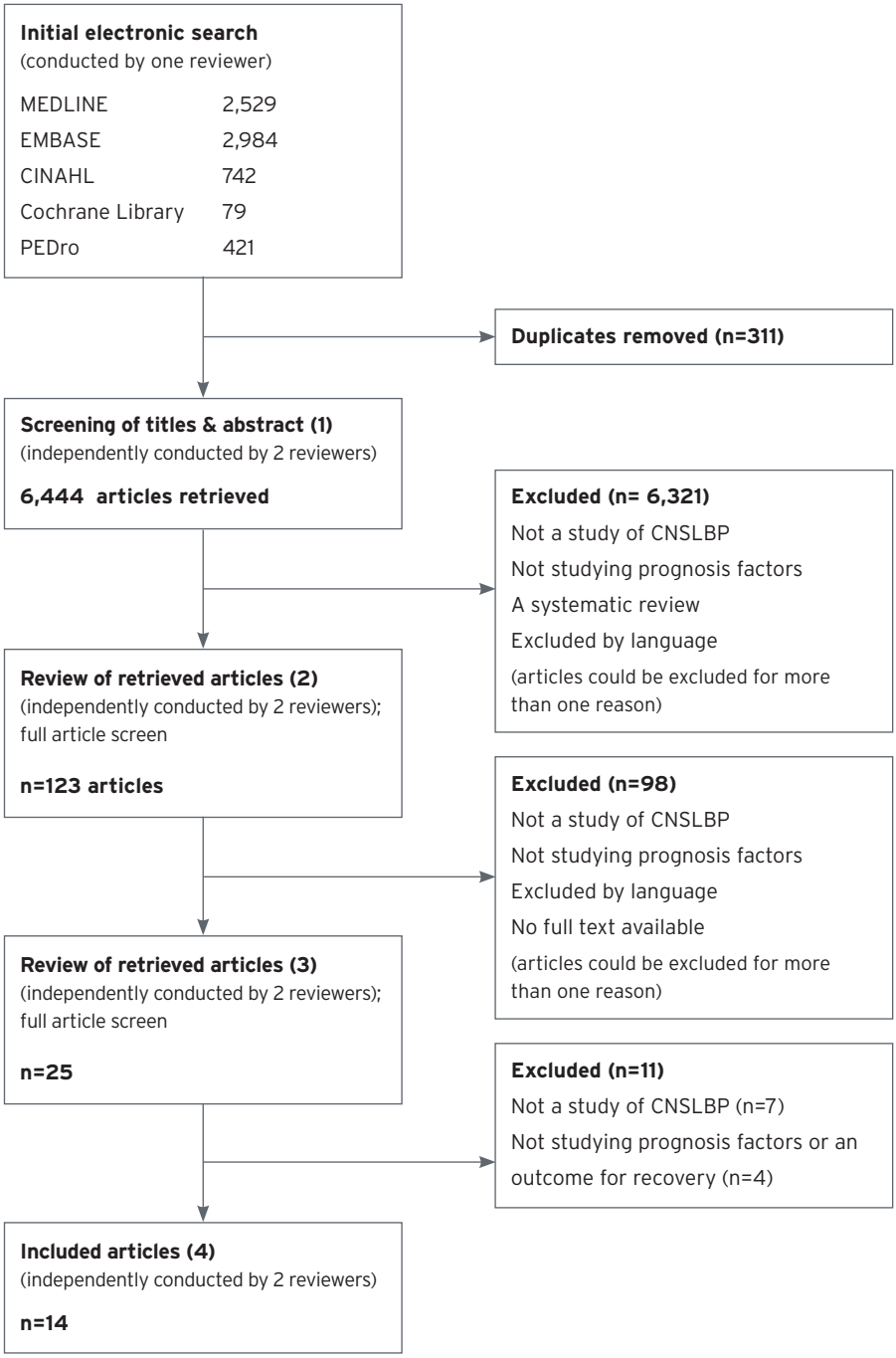

Figure 1. *Flowchart showing the search strategy*

CNLBP= chronic nonspecific low back pain

Methodological quality

The overall interobserver agreement was 80% for the methodological quality and 90% for the data extraction.

Table 2 presents the methodological quality scores (risk of bias) of all included studies. Ten studies were considered to be of low quality[19-21,23,25,27-31] and 4 studies were considered to be of high quality.[18,22,24,26] The methodological shortcoming most frequently noted were: no information about nonresponders versus responders, (item D) and no specified confounding measurement and no appropriate accounting of confounders (items J,K, and L) (Appendix 2). Nine of the 14 studies had no (or unclear) information about the presence of a prognostic model (item N).[19-25,28,29] Three studies[18,22,26] clearly defined one or more confounders (item J). Only 2 studies[30,31] provided information on the methods used to measure the confounders in a valid and reliable way (item K), and only 3 studies[18,22,24] applied appropriate accounting for confounding (item L). In addition to the score on prognostic factors and outcomes defined in the studies (item H and I), the reliability and validity of the instruments used to measure the prognostic factors and outcomes also were scored positive (low risk of bias) when consensus was reached by the reviewers.[19, 24, 25, 27, 28]

Prognostic factors and outcome measures

Table 3 presents the prognostic factors that were reported in only one study[18,20-31] The level of evidence for these prognostic factors was limited, or there was no evidence. A large number of different prognostic factors (n=77) were studied in relation to the outcomes of interest. A few prognostic factors showed some influence on improving or delaying the recovery, but most showed no association. Nine studies[20,22-27,30,31] had more than one outcome of interest.

Table 4 shows the 14 prognostic factors that were reported in at least 2 studies evaluating associations with the outcomes of pain intensity, disability, return to work, and quality of life.[18-31]

For 8 of the factors,[20,22-24,30,31] there was consistence evidence for no association. For 15 factors[18,20-28,30,31] there was conflicted evidence, and for 6 factors,[18,20,21,23,26] there was limited evidence for no association or positive influence. Seven out of 14 prognostic factors were reported by low quality studies.[20,21,23,25,27,30] The 4 high-quality studies reported either positive significance value or no significance value of factors on outcomes.[18,22,24,26]

It was not possible to present the strength and confidence interval of the associations due to poor presentation of the results in the studies. Contacting the authors did not provide additional information because the low response rate (one responded, but incorrectly).

Table 1. *Characteristics of the 14 included studies*[a]

Author	Design	Study Population	Setting	Recruitment	No. of Participants	Age (y) of participants	Follow-up measurements	% Lost to Follow-up
Anema et al b (2009)[18]	Prospective cohort study	Low back problems ≥ 3 mo	Six different countries, location not specified	May 1995 - September 1996	N=2,825, not reported	Not reported	1 and 2 y	First year 15%, second year 23%
Costa et al (2009)[23]	Inception cohort study (nested)	Chronic non-specific low back pain ≥ 3 mo	Primary care clinics in Sydney, Australia	November 2003 - July 2005	N=406; 214 men and 192 women	Mean 44.1 (SD= 14.5)	9 and 12 mo	Not described
Van der Hulst et al (2008)[30]	Randomised Controlled Trial	Non-specific chronic low back pain ≥ 3 mo (1) back rehabilitation and (2) usual Care	Outpatient multidisciplinary back rehabilitation program, "Het Roessingh", the Netherlands	Not specified	N=163; (1) back rehabilitation n=79 (47 men, 32 women) and (2) usual care n=84 (52 men, 32 women)	(1) Back rehabilitation mean 38 (SD =10), and (2) usual care Mean 40 (SD=10)	8 wk and 6 mo	n=21 (13%)
Keeley et al(2008)[27]	Prospective cohort study	Low back pain ≥ 6 mo	Orthopedic outpatient clinic	Not specified	N=120 (60 men, 60 women) (n=108 at baseline)	Mean 39.9 (SD=12.2)	6 mo	20% loss to follow-up for CSSR and 14% loss to follow-up for PCS of the 108 eligible participants
Chan and Chin (2008)[22]	Longitudinal retrospective correlation study	Chronic low back pain ≥ 3 mo	Canossa hospital, Hong Kong	2001-2006	N=178 (92 men, 86 women)	Mean 46.01 (SD=12.40)	6 and 12 wk	Unclear
Grotle et al (2006)[24]	Prospective inception cohort study	Acute and chronic low back pain: chronic for ≥ 3 mo	Back Clinic at Ostfold Hospital, Norway	Not specified	N=50 (19 men, 31 women)	Mean 40.4 (SD=9.5)	Patients with chronic low back pain: 6, 9 and 12 mo	n=3 (6%)
Koopman et al (2005)[28]	Prospective cohort study	Chronic low back pain	Institute of Vocational Assessment and Education, Rehabilitation Center Heliomare, the Netherlands	June 1998 - April 2001	N=68 (36 men, 32 women), n=51 at baseline (30 men, 21 women)	Mean 41.7 (n=51)	12 mo	n=13(19%)
Casso et al (2004)[21]	Prospective case series study	Chronic non specific low back pain ≥ 3 mo absence of work	Treatment and Rehabilitation Center of Orbe Hospital, Vaud Canton, Switzerland	June 1996	N=125 (115 men, 10 women)	Mean 40 (range= 23-59)	1 y	Not described

(continued)

Author	Design	Study Population	Setting	Recruitment	No. of Participants	Age (y) of participants	Follow-up measurements	% Lost to Follow-up
Woby et al (2004)[31]	Prospective cohort	Chronic low back pain ≥ 3 mo	Active, physical therapist-led rehabilitation program	Not specified	N=83 (46 men, 37 women)	Mean 41.1 (SD=10 SD)	8 wk	n=26 (31%) dropout and n=3 missing post treatment FABQ -W
Smith et al (2004)[29]	Prospective longitudinal study	CBP ≥ 3 mo: (1) persistent CBP and (2) recovered CBP	29 general practices in the Grampian region of Scotland	1996 baseline, 2000 follow-up	In 1996, N= 5,036 were approached In 1996, n=212 of the 3,605 participants had CBP In 2000, n=152 of the 1,608 participants had persistent CBP (over 4 years [1996-2000]) and n=252 had CBP in 2000 (first episode)	> 25-75	4 y	17%
Hagg et al (2003)[25]	Prospective multicenter, randomized controlled trial	Severe chronic Low back pain ≥ 2 y; surgical group (n=201) and nonsurgical group (n=63)	19 orthopedics departments, Sweden	1992-1998	N=294 (129 men, 135 woman at baseline)	Mean 43 (SD=8.3) (range= 25-65)	2 y	Unclear
Hansson and Hanssonb (2000)[26]	Prospective cohort study	Low back problems ≥ 3 mo	Six different countries, location not specified	Not specified	N= 2,752 (1,448 men, 1,304 women)	Mean 39-44 (SD= 9-11) (6 countries)	1 and 2 y	23.5%
Bendix et al(1998)[20]	Prospective clinical trial	Chronic disabling back pain for at least 6 mo	Copenhagen Back Center	June 1991 - June 1995	N=816; woman 67%-75%	Median for the 6 groups 40-42	1 y	15%
Barnes et al (1989)[19]	Retrospective case series	Chronic low back pain	Productive Rehabilitation Institute of Dallas for Ergonomics (PRIDE)	Not specified	N=150: (1) RTW n=60, (2) no RTW n=30, (3) non completers n=60 (men 105, 45 women)	Mean:(1) 36.9, (2) 39.9, (3) 35.6	1 and 2 y	0%

[a] *CBP=chronic back pain, CSSR= Client Socio-Demographic and Service Receipt Inventory, PCS= Physical Component Scale of the 36-Item Short-Form Health Survey questionnaire, FABQ-PA and FABQ-W= Fear-Avoidance Beliefs Questionnaire for physical activity (PA) and work (W) subscales, RTW=return to work.*

[b] *Articles of Anema et al and Hansson and Hansson report on the same study data.*

Table 2. *Results of the methodological assessment of the 14 reviewed studies*[a]

Study	Study participation	Study attrition (Follow-up)	Prognostic Factor	Outcome	Confounding Factor	Analysis	Quality
Anema et al (2009)[18]	Low	Low	Moderate	Low	Moderate	Low	High
Costa et al (2009)[23]	Low	Low	Low	Low	High	Low	Low
Van der Hulst et al (2008)[30]	Low	Moderate	Low	Low	High	Low	Low
Keeley et al (2008)[27]	Moderate	Low	Low	Low	High	Low	Low
Chan and Chin (2008)[22]	Low	Moderate	Low	Low	Moderate	Low	High
Grotle et al (2006)[24]	Low	Moderate	Low	Low	Moderate	Low	High
Koopman et al (2005)[28]	Moderate	Moderate	Low	Moderate	High	Low	Low
Woby et al (2004)[31]	Low	High	Low	Low	High	Low	Low
Casso et al (2004)[21]	Low	Low	Low	Low	High	Low	Low
Smith et al (2004)[29]	Moderate	High	Moderate	Moderate	High	Moderate	Low
Hagg et al (2003)[25]	Low	Moderate	Low	Low	High	Low	Low
Hansson and Hansson (2000)[26]	Low	Moderate	Low	Low	Moderate	Low	High
Bendix et al (1998)[20]	Low	Moderate	Moderate	Low	High	High	Low
Barnes et al (1989)[19]	Moderate	Moderate	Low	High	High	Low	Low

[a] *A study was rated for each of the 6 potential biases as low (Y,YYY, YYYY, YYYU, NYYY, NYYU), moderate (U, YUU,NYUU,NYYU,NNYY,NNYU), or high (N, NNU, NNUU, NNNY, NNNU NNNN) risk of bias per domain.*

The results are described for each outcome of interest for those prognostic factors whereby minimal one study of high quality was involved (table 4):

Pain intensity. In 7 studies,[20,22-24,26,29,31] pain intensity was the primary outcome. Six different instruments were used in these studies: visual analog scale (0-100mm),[22,31] numeric rating scale (0-10),[24] Von Korff pain score,[26] 6-point Likert scale,[23] a measure of pain severity of the back or leg. (0-10),[20] and the Chronic Pain Grade questionnaire.[29] Three studies were of high quality.[22,24,26]

Overall, the studies show consistent evidence that at short-term follow-up, age[22,31] and sex[22,31] were not predictive for pain decrease. The high-quality study by Chan and Chin[22] demonstrated a significant improvement for the change in pain at the 6- week follow-up associated with the baseline Fear-Avoidance Beliefs Questionnaire score (mean 27.73, SD 15.93), although accounting for only 3% of the variance in outcome. This finding was inconsistent with the findings at 8 weeks[31] and 12 weeks.[22]

Long-term follow-up provided consistent evidence that smoking[20,23,24] was not a predictive factor. Conflicting evidence was found for age,[20,24,26] sex,[20,24,26,29] and physical job demands[20,26] in association with pain intensity at the long-term follow-up; these studies were of low and high quality. Conflicting evidence also were found for sick leave[20,23,25,30] and work status,[20,23] but these studies were of low quality.

Disability. The Roland-Morris Disability Questionnaire[30,31] and the Oswestry Disability Index[24,25] were each used in 2 studies. Four studies[20,22,23,26] used other instruments to measure disability, including a 5-point Likert scale,[23] a physical impairment score (0-33),[22] a change in level of activities of daily living,[20] and the Hannover Activities of Daily Living Scale (0-100).[26] Three studies were of high quality.[22, 24, 26]

Consistent with the finding for the outcome pain for the short term, there was no association between the factors age and sex and the disability outcome.[24,31]

At short-term follow-up, conflicting evidence was found that fear-avoidance beliefs[22,30,31] were associated with disability. The study by Woby et al.[31] and the high-quality study by Chan and Chin[22] showed a positive association between the Fear-Avoidance Beliefs Questionnaire score and disability, although accounting for only 3% of the variance in outcome at 6 weeks. The positive association between the Fear-Avoidance Beliefs Questionnaire score and disability accounted for 12% of the variance in outcome at 12 weeks in the study by Chan and Chin.[22] Van der Hulst et al.[30] found no association between the Tampa Scale for Kinesiophobia-Dutch Version score and disability.

Table 3. *Prognostic factors and their outcomes each reported by only one study, at short-term and long-term follow-ups*[a]

Personal	Short Term	Long Term	Work (continued)	Short Term	Long Term
Age[27]		Q	Therapeutic work resumption[18]		R
Smoking[20]		R	Job redesign[18]		R
Duration of complaints[22,27]	P,D	R	Work adaptation[18]		R
Height[20]		P,D,R	Job strain[18]		R
Weight[20]		P,D,R	Longer tenure[18]		R
No. of adults at home[29]		P	Previous sick leave due to LBP[23]		P,D, R
Citizenship[21, 23]		D, R	Sick leave (days/months/many/few)[20,25,30]	D,Q	P,D,Q ,R
Health			Compensable LBP[18,23]		P,D,R
No surgery[18]		R	Work status[21,30]	D,Q	Q,R
Surgery[18]		R	Decision latitude (control)[26]		P,D,R
Comorbidity[18]		R	Psychological demands[26]		P.D,R
Cause of pain[27]		Q	Vibrations in the job[20]		P,D,R
Smoking[20]		R	**Physical**		
Vitality[26]		R	Physical job demands[20]		P,D,R
General health[23, 26]		P,R	ADL scores[20]		P,D
Coexisting of arthritis[29]		P	Sport activities[20]		P,D,,R
Currently taking medication for LBP[18,23]		P,D,R	Aerobic capacity[20]		P,D,R
Treatment before sick-listing[26]		P,D,R	Mobility[20]		P
Treatment(s) during present problems(e.g., LBP)[26]		P,D.R	Strength[20]		P,D
Treatment[18, 30]	D,Q	D,Q,R	Disability level at chronic presentation (SF-36)[23]		P,D
Treatment x sick leave[30]	D,Q	D,Q	Functional disability[28]		R
Treatment x SCL-90-dep[30]	D,Q	D,Q	Disability at acute or chronic presentation[23]		P, D
Treatment x work status[30]	D,Q	D,Q	**Psychological health**		
Treatment X TSK[30]	D,Q	D,Q	MPI-DLV[30]	D,Q	D,Q
Treatment x MPI-DV[30]	D,Q	D,Q	TSK[30]	Q	
Treatment x pain[30]	D,Q	D,Q	FABQ (0-96) / FABQ- PA and FABQ-W[24]		P

(continued)

Pain	Short Term	Long Term	Psychological health (continued)	Short Term	Long Term
Pain			Catastrophizing subscale of the CSQ[31]	P,D	
Age when first back pain[20]		P,D,R	Control over pain (CSQ)[31]	P, D	
Perceived risk of persistent pain[23]		P,D	Ability to decrease pain (CSQ)[31]	P,D	
Pain intensity at acute or chronic presentation[23]		P,D	Feelings of depression (SCL-90-dep/ZDS)[23,25,30]	D,Q	P,Q,G
Back pain level[20]		P,D,R	HADS[27]		Q
Leg. pain level[20]		P, R	Distress[24]		P,D
Distribution of the pain: localized vs diffuse[21]		R	Back pain-related Social stresses[27]		Q
Reinterpretation of pain sensation[28]		R	Back pain-independent social stresses[27]		Q
Pain intensity[30]	D,Q	Q	Level of expressed need[29]		P
Social			**Cognitive factors**		
Education[23,27]		P,D, Q	Mental health[26, 29]		P,R
Social functioning[26]		R	**Others**		
Social status[20]		D,R	Overall evaluation by patient: disappointing vs failure[21]		R
Work			Overall evaluation by patient: satisfaction vs failure[21]		R
Work hours adaptation[18]		R	''Red flag'' symptoms[23]		P, D

[a] *P= pain intensity, D= disability, R=return to work, Q= Quality of life, G=global assessment patient, LBP = low back pain, ADL= activities daily living,SF-36= 36-item Short-Form health Survey questionnaire, MPI-DLV = Multidimensional Pain Inventory-Dutch Language Version, TSK = Tampa Scale for Kinesiophobia, FABQ- PA = Fear-Avoidance Beliefs Questionnaire for physical activity (PA), FABQ -W= Fear-Avoidance Beliefs Questionnaire for work (W), CSQ= Coping Stategies Questionnaire, HADS = Hospital Anxiety and Depression Scale, SCL-90-dep= Symptom Checklist-90 depression subscale, ZDS=Zung Depression Scale.*

Table 4. *Prognostic factors and their outcomes of interest (≥ 2 studies) at short-term and long-term follow-ups*[a]

Group	Prognostic Factor	Outcome	Short Term	Long Term	+ High Quality	+ Low Quality	0 High Quality	0 low Quality	- low Quality	Evidence
Personal	Age	Pain	X				1[22]	1[31]		Consistent
		Pain		X	1[26] (a-f)	1[20] (F/C)		1[24]		Conflicted
		Disability	X				1[22]	1[31]		Consistent
		Disability		X	1[26] (a-f)		1[24]	2[20] (F/C)[25]		Conflicted
		RTW		X	1[26] (a,b,c,e)	2[20] (F/C)[28]	1[26] (d,f)	1[21]		Conflicted
	Sex	Pain	X				1[22]	1[31]		Consistent
		Pain		X	1[26] (a)	1[20] (C)	2[24, 26] (b-f)	2[20] (F)[29]		Conflicted
		Disability	X				1[22]	1[31]		Consistent
		Disability		X	1[26] (a,c,d,e)		2[24, 26] (b,f)	1[20] (F/C)[25]		Conflicted
		RTW		X	1[26] (a,b)	2[20] (F/C)[28]	1[26] (c,d,e.f)	1[25]		Conflicted
	Smoking	Pain		X			1[24]	2[20] (F/C)[23]		Consistent
		Disability		X			1[24]	2[20] (F/C)[23]		Consistent
Pain	Leg. pain level	Disability		X				2[20] (F/C)[23]		Limited
	Pain intensity β (lower)	Disability		X			1[24]	1[30] (*,%)		Consistent
		RTW		X	2[18, 26] (a-f)			1[21]		Limited
Social	Social work	Pain		X				2[20] (F/C)[23]		Limited
Work	Sick leave (days/months)	Disability		X				3[23, 25, 30] (*,%)	1[20] (F/C many)	Conflicted
	Work status	Pain		X				2[20] (C back pain), (F)[23]	1[20] (C leg. pain)	Conflicted
		Disability		X				2[20] (C)[30] (*,%)	1[20] (F)	Conflicted

(continued)

Group	Prognostic Factor	Outcome	Short Term	Long Term	+ High Quality	+ Low Quality	0 High Quality	0 low Quality	- low Quality	Evidence
Physical	Physical job demands (lower)	Pain		X	1[26] (c,d)	1[20] (F/C leg. pain)	1[26] (a,b,e,f)		1[20] (F/C back pain)	Conflicted
		Disability		X	1[26] (e)		1[26] (a,b,c,d,f)	1[20] (F/C)		Conflicted
		RTW		X	2[18, 26] (a-f)			1[20] (F/C)		Limited
	ADL scores	RTW		X	2[18, 26] (a,c,e)		1[26] (b,d,f)	1[20] (F/C)		Conflicted
	Mobility §	Disability		X				2[20] (F/C)[23]		Limited
		RTW		X		1[28]		2[20] (F/C)[21]		Conflicted
	Strength ¶	RTW		X				2[20](18) (F/C)[21](19)		Limited
Psychological health	TSK/FABQ FABQ-PA and FABQ-W	Pain	X		1[22]		1[22]	1[31]		Conflicted
		Disability	X		1[22]	1[31]		1[30] (*, %)		Conflicted
		Disability		X			1[24]	1[30] (*,%)		Consistent
		Quality of life		X		1[30] (%) P		2[27, 30] P/M, (%)		Conflicted
	Feelings of depression (SCL-90)	Disability		X				2[23, 30] (*)	1[30] (%)	Conflicted
No data available		Disability	X[25]							
		RTW		X[19, 23]						

[a] *0 = not significant, + = significant positive, - = significant negative, RTW=return to work. Subgroups in the study by Hansson and Hansson[26] : a= Denmark, b= Germany,c= the Netherlands, d= Sweden, e= United States, f= Israel.Study by van der Hulst et al[30]: regardless of treatment (*), with interaction of treatment (%), P= Physical Component Scale of the 36-Item Short-Form Health Survey questionnaire, M= Mental Component Scale of the SF-36; MPI-DLV, Multidimensional Pain Inventory-Dutch Language Version. Study by Bendix et al[20] : F = multidisciplinary treatment, C = back school group. § mobility: Costa et al,[23] persisting limitation of spinal movements in all directions; Bendix et al,[20] mobility; Casso et al,[21] finger-to-floor distance; Koopman et al,[28] trunk flexibility. strength : Casso et al,[21], Biering-Sorensen test; Bendix et al,[20], isometric abdominal endurance and isometric back endurance. β visual analog scale, numeric rating scale, MPI-DLV, Tampa Scale for Kinesiophobia (TSK), Fear-Avoidance Beliefs Questionnaire for physical activity (FABQ- PA) and Fear-Avoidance Beliefs Questionnaire for work (FABQ-W), Coping Stategies Questionnaire, Hospital Anxiety and Depression Scale and Symptom Checklist-90 (SCL-90).*

The study by Hagg et al.[25] had a 2-year follow-up period and demonstrated no association for improvement in all the assessed factors, but they did not present the data. The high-quality study by Hansson and Hansson[26] demonstrated that in 6 countries a lower age was associated with more improvement in disability scores over a longer follow-up period (> 1 year). In 4 out of 6 countries, male sex showed a positive association with improvement in disability scores.[26] The high-quality study by Grotle et al.[24] and the low quality studies by Bendix et al.[20] and Hagg et al.,[25] however, demonstrated no associations with age or sex for the long-term follow-up. Also, at long-term follow-up, conflicting evidence was found for an association between physical job demands[20,26] and disability. There was consistent evidence that smoking,[20,23-25] pain intensity at baseline,[24,30] and fear-avoidance beliefs[24,30] were not associated with more improvement in disability scores on long-term follow-up.

Return to work. The work-related variables included work status,[23,25] work resumption,[26] return-to-work,[18,19,21,28] and ability to work.[20] Two studies were of high quality.[18,26] All studies reported on prognostic factors at the long-term follow-up, but these were scored with different instruments.
In 2 out of the 3 studies of high quality, lower pain intensity[18,21,26] and lower physical job demands[18,20,26] at baseline showed limited evidence of returning to work earlier.

Conflicting evidence was found for age,[20,21,26,28] sex,[20,25,26,28] and daily activities,[18,20,26] with at least one high-quality study represented.

Three studies reported that younger age predicted return to work.[20,26,28]

Quality of life. The low-quality studies by van der Hulst et al.[30] and Keeley et al.[27] used the Physical Component Scale of the 36-Item Short-Form Health Survey questionnaire (SF-36) but investigated different prognostic factors. Therefore, each factor was limited to no evidence (table 3). For the factor fear-avoidance beliefs, both studies[27, 30] showed conflicted evidence for the long term follow-up (Table 4).

Patient global assessment. Because only one study[25] of low quality included patient global assessment, the evidence was restricted (Table 3).

Discussion

This systematic review aimed to present potential prognostic factors that can influence relevant outcomes such as pain intensity, disability, return to work, quality of life and global perceived effect in patients with CNLBP.

The evidence for each association of a prognostic factor with any outcome variable was weak, and most studies were of poor methodological quality. Only 2 to 5 studies reported on the same prognostic factors.

Moreover, the confidence intervals of the odds ratios (if reported) were generally widespread, indicating uncertainty in the estimation of association. Therefore, caution is needed in the interpretation of these results.

Prognostic factors and outcomes

In the included studies, pain intensity, disability, and return to work were the most frequently reported outcomes, similar to the reviews on acute NLBP and the transition from acute to chronic NLBP.[4,5,15,32,33] Comparison with these studies is difficult because few studies are available and the clinical course of CNLBP can differ between acute and subacute NLBP.[9,15,34] However, criticisms of the use of different instruments for the same prognostic factors, the timing of follow-up measurements, and unclear definitions of outcomes were similar between the available systematic reviews[4,6,7,15,32] and the present review.

For the outcomes of pain and disability, several studies[20,22,24,25,30,31] implied that there can be a correlation or interaction between these 2 outcomes and the investigated prognostic factors. Different kinds of possible bias were present, including lack of a control group to reflect the natural course,[24,31] small sample size,[24,25,31] no blinded measurements,[23] and self-reporting by the patient.[23] Therefore, the possible relation between pain en disability, the quality of the instruments, and the various biases in the studies indicated that the results should be interpreted as a direction for further research.

For the outcome return to work, aspects such as small sample size[21,25] and self-reported sick leave absence[28] can reduce the validity of the results. The outcomes quality of life and patient global assessment were not investigated in any studies of high quality. The available studies suffered from difficulties with the results due to a small percentage of patients at work (20%)[30] and the possible interaction with pain intensity and disability[27] that could influence the results. Therefore, future research needs to have a sufficiently large sample size, measure the potential prognostic factors with similar instruments, and use well-defined outcomes of interest.

Researchers should incorporate the quality assessments of the 6 bias domains into their synthesis of evidence about prognosis. The inclusion and exclusion criteria for patients with CNLBP should be clearly defined, and there should be several follow-up periods (at least 1 year). These suggestions will provide the opportunity to investigate the course of CNLBP and to identify modifiable prognostic factors on outcomes. To improve the quality of the prognostic studies the following considerations are important: (1) precisely defining the study objectives, (2) presenting the study methods and data, and (3) interpreting and applying the results of the study.[35]

Limitations and methodological quality

An important strength of this review is that the evidence regarding prognostic factors in outcomes of CNLBP is now systematically summarised, showing evidence available and the areas in which further research is needed.

In the present review, problems arose in identifying the prognostic factors and associations with outcomes and in reporting the predictive strength of associations due to: (1) searches made in different databases, (2) variation in the study design (heterogeneity), (3) inadequate description of the selection criteria; and (4) insufficient methodological quality of most of the studies.[1,4]

Haynes et al.[4] suggest that at least MEDLINE and EMBASE should be used in a search for articles of prognostic value. Although we used MEDLINE, CINAHL, EMBASE, the Cochrane Library, and PEDro some relevant studies may not have been included in these databases. Therefore, the possibility of publication bias cannot be ruled out.[1]

We chose to include randomized cohort study designs, which gave a large variety of prognostic factors and outcome measures. Some results were based on data from study designs (e.g., randomized controlled trails) that initially were not designed to identify prognostic factors for CNLBP improvement. Another form of heterogeneity could lie with the definition of the study population; all 14 studies described their selection criteria, but no study provided a clear definition or diagnostic labeling of patients with CNLBP.

The criteria list we used for quality assessment was based on the QUIPS low back pain tool by Hayden.[14] The main reasons for modifying the QUIPS list was the length of the list and the items we considered most relevant for the current topic; however, the 6 domains for risk of bias are presented. A specific cutoff point for high quality or low quality is difficult to define (even when based on theoretical considerations) and thus remains arbitrary. The most frequent topic of discussion between the present authors was whether the included studies clearly or completely described the reliability and validity of the method of measurement of the prognostic factors, outcomes, and confounders. A second major topic was which factors can be described as prognostic and which factors can be described as confounders, because they were seldom explicitly defined in the included studies. These matters may have influenced the quality scores and the interpretation of the results.

Apart from the low methodological quality of most of the studies, it was difficult to report the qualitative results of the studies due to problems with different measures of prognostic factors and confounders, poor statistical methods, and different ways of reporting the outcomes.

Implication for clinical practice

This systematic review revealed that there is little consistent evidence as to which prognostic factors are of value in the recovery from CNLBP. There is no consistent evidence that any positive prognostic factors are associated with one of the investigated outcomes.

At short-term (≤ 6 months) follow-up there was consistent evidence for no association regarding the prognostic factors age[22,31] and sex[22,31] for pain intensity and disability. Smoking[20,23,24] had the same result on the long-term (> 6 months) follow-up. Pain intensity[24,30] and fear of movement[24,30] had no association on the long term with the outcome disability.

Conflicting evidence was found for the association between the outcomes pain intensity and disability at the short term follow-up for the prognostic factor fear of movement.[22,30,31] On the long-term follow-up, conflicting evidence was found for the factors age[20,24-26], sex[20,24-26,29] and physical job demands.[20,26]

Conflicting evidence was found for the association between return to work and age,[20,21,26,28], sex,[20,25,26,28] and activities daily lives[18,20,26] at long-term follow-up.
At baseline, limited evidence of a positive influence on return to work was found for lower pain intensity[18,21,26] and physical job demands.[18,20,26] No studies of high quality were found for the outcome of quality of life and global perceived effect.[25,27,30]

This review provides evidence-based information that may be valuable to clinicians and policymakers in guiding their professional practice and suggest that more studies are needed to further clarify these unclear and conflicting results on prognostic variables in patients with CNLBP, especially those prognostic factors that can be influenced by the clinicians or the patients.

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Appendix 1

Full Search Strategy for Prognostic Factors in Chronic Nonspecific Low Back Pain for Recovery in MEDLINE/PUBMED (1966-March 2010)[a]

Phase 1: Sensitive search for low back pain

1. Back pain
2. Low back pain
3. Simple back pain
4. Nonspecific low back pain
5. #1 OR #2 OR #3 OR #4

Phase 2: Sensitive search for prognosis

6. Prognosis
7. Prediction
8. Course

Phase 3: Sensitive search for outcome

9. Outcome assessment
10. Outcome treatment
11. Recovery

Phase 4: Sensitive search for design

12. Cohort studies
13. Follow-up studies
14. Longitudinal studies
15. Prospective studies
16. Controlled clinical trials
17. Randomized controlled trials
18. Case-control studies
19. Retrospective studies
20. Case studies
21. Search #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20

Phase 5: Exclude criteria and limits

22. Intervertebral disk displacement
23. Infection
24. Neoplasm
25. Neoplasm metastasis
26. Cancer
27. Arthritis

28. Arthritis rheumatoid
29. Arthritis juvenile rheumatoid
30. Fibromyalgia
31. Fracture
32. Osteoporosis
33. Pregnancy
34. Reiter disease
35. Diskectomy
36. #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35
37. #5 NOT #36
38. #37 AND #21
39. #38 AND chronic
40. #39 Limits: Humans, English, Danish, Dutch, Norwegian, Swedish

MEDLINE: 2,529, CINAHL: 742, EMBASE: 2984, Cochrane Library: 79, PEDro: 421

[a] *Search Stategies were modified appropriately by reviewer (K.V.) for EMBASE (1950-March 2010), CINAHL (1984-March 2010), Cochrane Library (Cochrane Central Register of Reviews, trials to March 2010) and PEDro (1929-March 2010).*

Appendix 2

Criteria List for Assessing Methodological Quality

1.1 Study participation

A. Description of study population
B. Description of inclusion and exclusion criteria
C. Description of baseline study population

1.2 Study attrition, Follow-up (extent and length)

D. Information about nonresponders versus responders
E. Follow-up of at least ≥ 3 months
F. Drop-outs/loss to follow-up ≤ 20%
G. Information completers versus loss to follow-up/drop-outs

1.3 Prognostic factors measurement

H. Clearly defined constructs of what is measured was provided, standardised assessment of patient characteristics and potential clinical prognostic factors

1.4 Outcome measurement

I. Clearly defined and standardised assessment of relevant outcome criteria: pain, disability, quality of life, return to work, global perceived effect

1.5 Confounding measurement and account

J. Important confounders measured
K. Valid and reliable measurement of confounders
L. Appropriate accounting for confounding

1.6 Analysis

M. Appropriate analysis techniques
N. Prognostic model presented
O. Frequencies of most important prognostic factors
P. Frequencies of most important outcome

CHAPTER 3

Course and prognosis of recovery for chronic non-specific low back pain: design, therapy program and baseline data of a prospective cohort study

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BMC Musculoskelet Disord 2011,12:252

Abstract

Background. There has been increasing focus on factors predicting the development of chronic musculoskeletal disorders. For patients already experiencing chronic non-specific low back pain it is also relevant to investigate which prognostic factors predict recovery. We present the design of a cohort study that aims to determine the course and prognostic factors for recovery in patients with chronic nonspecific low back pain.

Methods/ Design. All participating patients were recruited (Jan 2003-Dec 2008) from the same rehabilitation centre and were evaluated by means of (postal) questionnaires and physical examinations at baseline, during the 2-month therapy program, and at 5 and 12 months after start of therapy. The therapy protocol at the rehabilitation centre used a bio-psychosocial approach to stimulate patients to

adopt adequate (movement) behaviour aimed at physical and functional recovery. The program is part of regular care and consists of 16 sessions of 3 hours each, over an 8-week period (in total 48 hours), followed by a 3-month self-management program. The primary outcomes are low back pain intensity, disability, quality of life, patient's global perceived effect of recovery, and participation in work. Baseline characteristics include information on socio-demographics, low back pain, employment status, and additional clinical items status such as fatigue, duration of activities, and fear of kinesiophobia. Prognostic variables are determined for recovery at short-term (5 months) and long-term (12 months) follow-up after start of therapy.

Discussion. In a routine clinical setting it is important to provide patients suffering from chronic non-specific low back pain with adequate information about the prognosis of their complaint.

Background

In the Netherlands, the annual incidence of back pain in the general population is estimated at 10-15%.[1] In 1999, chronic non-specific low back pain (CNLBP) was reported by 16.0% of Dutch working men, by 23.1% of non-working men, by 17.9% of working women and 27.4% of non-working women.[2] CNLBP has consequences for daily activity, use of health care services and ability to work. Most people with acute low back pain recover from their pain and/or disability and return to work within a few weeks.[3] Up to 3 months the self-limiting condition improves at a slower pace compared to the first month of recovery, and after 3 months the chance of recovery diminishes for patients with CNLBP.[1,3-5] However, CNLBP can fluctuate over time with (frequent) recurrences or exacerbations.[6,7] Identifying the factors that predict the prognosis of CNLBP can help physicians in the management of patients with CNLBP. Prognostic factors are suspected to differ between acute and chronic non-specific low back pain since the course of these two conditions differs.[4,8] The transition from acute non-specific low back pain to CNLBP has been well investigated[9-12], whereas studies on prognostic factors for recovery from CNLBP are scarce.

A recent systematic review investigating which outcome measurements were used to define recovery of low back pain in the past 10 years, concluded that almost every study defined recovery differently.[13] Although pain and disability were the outcome measurements most often used for defining recovery, a broader perspective may provide a more comprehensive health profile of the patient.[14-16]

Therefore, we present the design of a cohort study that investigates the course of patients with CNLBP undergoing treatment in an outpatient rehabilitation centre.

Also investigated are prognostic factors for recovery using the outcomes low back pain intensity, low back pain specific disability, generic health status, patient's global perceived effect of recovery and work participation on both the short (5-month) and long (12-month) term.

Methods/Design

Design

This study is a prospective cohort study. Patients were recruited (from January 2003 – December 2008) in a multidisciplinary outpatient rehabilitation clinic the 'Spine & Joint Centre' (SJC) in Rotterdam. The Medical Ethics Committee of SJC approved the study and all participants provided informed consent.

Participants

In the present study, low back pain is defined as 'non-specific low back pain', i.e. low back pain without a specified physical cause, such as nerve root compression (the radicular syndrome), trauma, infection or the presence of a tumour. Pain in the lumbosacral region is the most common symptom in patients with non-specific low back pain. Pain may also radiate to the gluteal region or to the thighs, or to both.[17]

Patients with CNLBP (low back pain duration > 3 months) not recovering after primary and/or secondary care were referred by their general practitioner (GP) or specialist to the SJC for a diagnostic consultation.

The inclusion criteria for this study are:

- Men and women aged 18 years or over;
- Having CNLBP (i.e., a duration of low back pain for ≥ 3 months);
- Previous and insufficient treatment in primary and secondary care (e.g., physiotherapy);
- Signed informed consent.

Exclusion criteria are:

- Insufficient knowledge of the Dutch language;
- Signs indicating radiculopathy: asymmetric Achilles tendon reflex and/or (passive) straight leg raise test restricted by pain in the lower leg; positive magnetic resonance imaging findings for disc herniation;
- Recent (< 6 months) fracture, neoplasm or recent previous surgery (< 6 months) of the lumbar spine, the pelvic girdle, the hip joint, or the femur;
- Specific causes such ankylosing spondylitis and systemic disease of the locomotor system;
- Being pregnant or ≤ 6 months post-partum at the moment of consultation.

Procedure in the SJC

Based on a bio-psychosocial understanding of CNLBP the following steps are followed (Figure 1):

Intake (diagnostic consultation).

The intake is a 3-hour session in which: 1) the patient fills in psychometric questionnaires by computer; 2) a recording is made of the patient's strength (Isostation B200), a motion analysis of forward bending of the lumbar pelvic rhythm (video registration) of the trunk, and 3) the patients sees a physician for history taking and physical examination. The physician may request an additional consultation with a psychologist and/or manual physiotherapist before deciding on treatment management.

Patients meeting the inclusion criteria for the SJC are invited to participate in the multidisciplinary treatment program. Those not wishing to participate in this program are referred to their GP with a letter containing appropriate recommendations.

Therapy program.

In the therapy protocol, behavioural principles are applied to stimulate patients to adopt adequate normal behavioural movement aimed at physical recovery. The program consists of 16 sessions of 3 hours each, over a 2-month period (a total of 48 hours) located in the SJC. During the program patients are educated to be self-supporting and to become 'their own therapist'. After this 2-month period, patients are stimulated to continue the training program independently for at least 3 months, twice a week, in a local, regular health centre located near their home environment. Five months after the start of the therapy program (2 months at SJC + 3 months self-supporting activity) the patient has a follow-up meeting.

5-month follow-up after start of therapy.

At the 5-month follow-up the patient fills in questionnaires, and discusses the recovery process with a focus on personal targets with regard to physical training, and psychological and social factors. A physical examination takes place and (if required) personal advice is provided by one of the therapists of the SJC.

12-month follow-up after start of therapy.

Via postal correspondence the patient is asked to fill in the 12-month questionnaires. At the SJC a small group of patients follow treatment once a week for 4 months (instead of twice a week for 2 months). After the program is completed they are encouraged to continue their training program for at least 3 months in a regular health centre. At 7 and 14 months after start of therapy the same follow-up procedure is performed. The reason for the 'once a week' program is that some patients are unable to visit twice the SJC a week due travelling and/or physical problems.

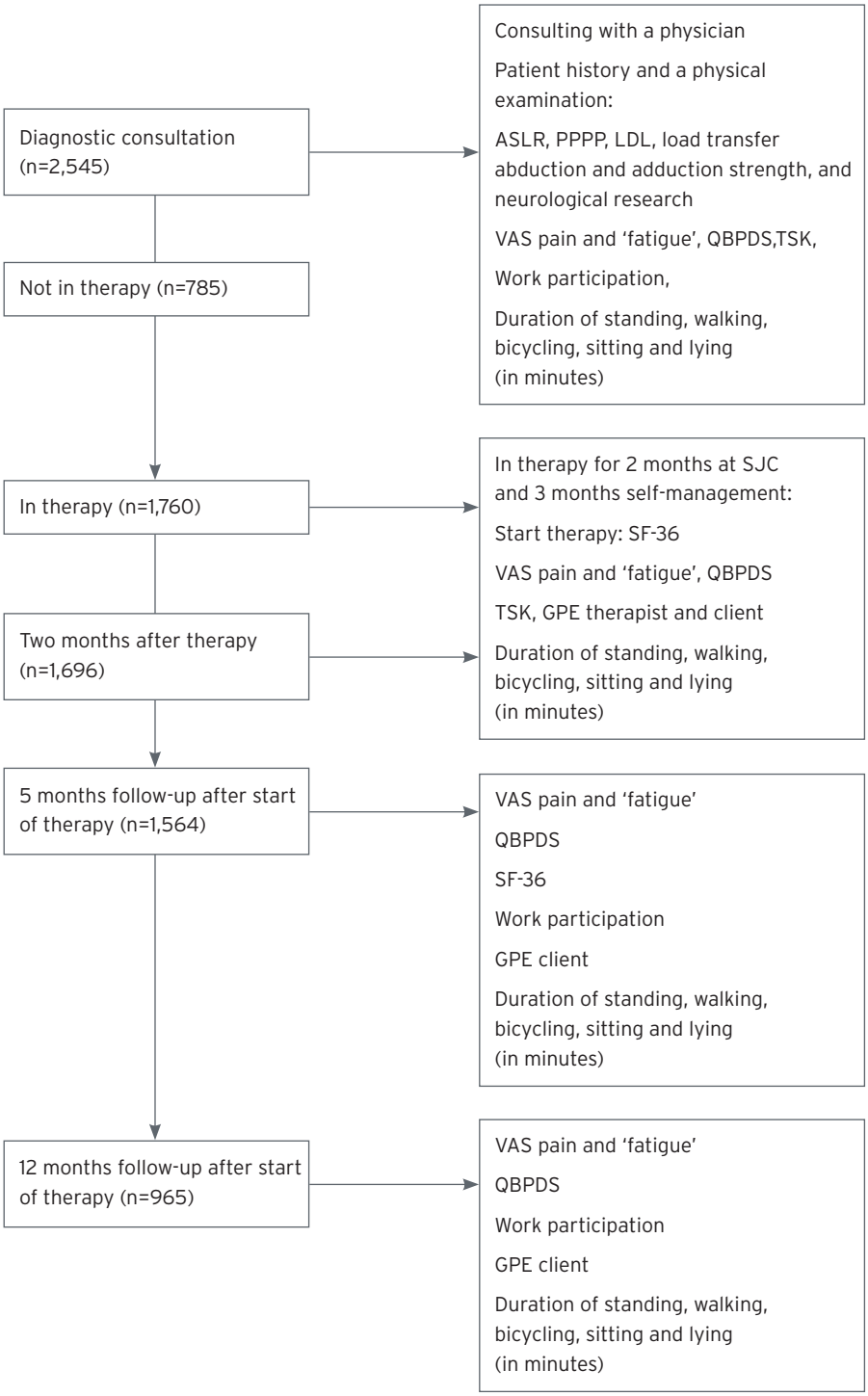

Figure 1. *Study design*

ASLR= Active Straight Leg Raise test; PPPP= Posterior Pelvic Pain Provocation test; LDL= long dorsal sacro-iliac ligament; VAS= Visual Analogue Scale; QBPDS= Quebec Back Pain Disability Scale; SF-36=Short Form; TSK= Tampa Scale Kinesiophobia.

SJC treatment program

Patients are treated in groups of 6 accompanied by 3 therapists. In the first session a personal treatment goal/plan is established with agreement from the patient. During the 9th and 16th sessions there is a 1:1 patient/therapist evaluation (in addition to the regular training program). The remainder of the treatment sessions consist of 1-hour training, a 1-hour group lesson, followed by another 1-hour training. The training consists of group training and/or individual coaching. Figure 2 presents the treatment protocol. The therapists (e.g., a physiotherapist, Mensendieck therapist, psychologist, health scientist, physician) are trained in the bio-psychosocial aspects of CNLBP.

The aim of the program is to normalise motion behaviour. This is done by modifying the patient's experience of movements and increasing the experienced quality of movements by learning about and training the reduction of compensatory mechanisms of a physical nature, e.g. increasing intra-abdominal pressure at low loads, breathing cessation during loading tasks, and extreme activity in all superficial muscles. During the program it is explained that the above-described compensatory mechanisms are present due to an interaction between biophysical and psychosocial factors (multidimensional) such as stress, psychological status and social factors. All these factors are treated by a multidisciplinary team.

The training starts to increase awareness of excessive tension of the muscles in trunk and extremities. The patient is stimulated to take breaks during daily activities by using tools like time contingent management and learning about his/her physical load and physical capacity.[18,19] Breathing techniques are used in combination with a stabilisation program to normalise the activity of the m. Multifidus, m. Transversus abdominis[20-25], diaphragm and pelvic floor (the 'inner tube system'). In a later stadium different coordination patterns of the lumbar-pelvic rhythm by sitting, standing, stooping and walking are experienced by the patient, and through strengthening exercises of the 'global muscles' (the 'outer tube system') the local load of the trunk is increased.[26-28] Cardiovascular endurance is trained by a cardio program. The daily activities of the patients are built up, depending on the physical load that the patient can bear.

The lessons aim to modify the patient's cognitions with respect to their complaints, thus reinforcing well behaviour.[29] The group lessons include information on the patient's activities, functional anatomy of the spine, principles of chronic pain, the role and impact of emotions, communication, and finding the balance between the load of daily life and physical capacity.

Individual coaching focuses on the specific needs/problems of the patient. The training is performed in a progressive sequence adjusted to the patient's situation and the clinical experience (estimation) of the therapist. Additional assistance (as required) is provided by a manual therapist, psychologist or therapist specialised in body awareness.

Session 1

1. Intake consultation between patient and therapist:
   a. screening by questionnaires, and patient's goals
   b. patient receives an information map
   c. screening if there is a problem with the pelvic floor
   d. patient is informed of the time contingent load
   e. personal goals are created for the patient and his/her motivation for the therapy
2. Introductory lesson (1 hour), a video is made of the patient's activities and his/her strength (rotation and extension) is measured

Sessions 2-8

1. Target: training the patient's cognitions and physical aspects
2. Parts of the therapy: (2 x 45 min)
   a. physical awareness and relaxation
   b. stabilization program
   c. cardio program (walking, bicycling, rowing)
   d. strength exercises (force closure)
3. Lessons on: anatomy (2x), pain and pain experience, physical load, attitude and movement in daily life (2x), emotions
4. The multi-dimensional load-carrying capacity model and behaviour change

Session 9: Evaluation at SJC

1. Target: evaluation therapy
   a. questionnaires (QBPDS and TSK, VAS pain and fatigue)
   b. personal goals of the patient and their motivation
2. Parts of the therapy: (2 x 45 min)
   a. physical awareness and relaxation
   b. stabilization program
   c. cardio program (walking, bicycling, rowing)
   d. strength exercises (force closure)
3. Lesson: group evaluation and relaxation exercises
4. Patient thinks about the phase after the program has ended

Sessions 10-15

1. Target: patient becomes own coach
2. Parts of the therapy: (2 x 45 min)
   a. physical awareness and relaxation
   b. stabilization program
   c. cardio program (walking, bicycling, rowing)
   d. strength excises (force closure)
   e. daily activities are built up
3. Lessons on: pelvic floor and a second pregnancy, preparing oneself for self-training, movement in daily life, communication, intimacy and sexuality, anatomy, pain and how to handle recidivism
4. Building-up daily activities

Session 16: Evaluation at SJC

1. Target: evaluation of therapy program and personal goals
2. Parts of the therapy: (1 x 45 min)
   a. physical awareness and relaxation
   b. stabilization program
   c. cardio program (walking, bicycling, rowing, cross trainer)
   d. strength excises (force closure)
   e. daily activities are built up
3. Lesson: group and individual evaluation
4. Testing patient's strength; filling in and discussing questionnaires (QBPDS, TSK, VAS pain and fatigue, GPE patient)

Self-management for 3 months

1. Target: continuing therapy program and personal goals twice a week in a local 'fitness' centre
2. Parts of the therapy:
   a. physical awareness and relaxation
   b. stabilization program
   c. cardio program (walking, bicycling, rowing, cross trainer)
   d. strength excises (force closure)
   e. daily activities are built up
3. Evaluation at the SJC 5 months after start of therapy (2 months SJC and 3 months self-management); filling in/discussing questionnaires (QBPDS, TSK, VAS pain and fatigue, GPE patient).
4. Physical examination: ASLR, PPPP, LDL, load transfer abduction and adduction strength.

Figure 2. *Flow chart of the therapy program*
VAS= Visual Analogue Scale; QBPDS= Quebec Back Pain Disability Scale; SF-36=Short Form; TSK= Tampa Scale Kinesiophobia; GPE=Global Perceived Effect; ASLR= Active Straight Leg Raise ; PPPP= Posterior Pelvic Pain Provocation test; LDL= Long Dorsal sacro-iliac Ligament.

Prognostic factors

Prognostic factors are assessed at intake and at start of therapy by means of an interview focusing on the patient's history, a physical examination, and on questionnaires. After the 2-month therapy program at SJC, post-treatment follow-up measurements are scheduled at 5 and 12 months after start of therapy. In the present study, the classification into domains as proposed by Pincus et al., with one additional domain 'Physical characteristics', is used to order the prognostic factors.[30]

Table 1 lists the prognostic factors. The prognostic factors include: a) *demographic characteristics* such as educational level, marital status, weight, alcohol, smoking and drug consumption; b) *clinical status* such as body mass index (BMI), pain below the knee, cause and duration of complaints, previous rehabilitation, degree of fatigue[31], low back pain intensity (VAS)[32,33] and disability

(QBPDS).[34,35]; c) *psychological characteristics* such as fear avoidance (TSK)[36-42] and quality of life (SF-36)[43]; d) *work-related characteristics* such as employment benefits and work participation in relation to back complaints, and e) *physical characteristics* such as the mobility of lumbar pelvic rhythm (video registration)[44], strength (B-200 isostation)[45,46] and activities of daily living (ADL) consisting of walking, sitting, bicycling and lying. Figure 1 shows the physical tests that are measured at intake, evaluated at the end of therapy, and at 5 months after start of therapy. The reliability and validity of these tests have been established. The Active Straight Leg Raising (ASLR) test[47-49] (0= not difficult at all, 1= minimally difficult, 2= somewhat difficult, 3= fairly difficult, 4= very difficult, 5= unable to do) is positive when the bilateral sum score is ≥ 2 (score range 0-10). The posterior pelvic pain provocation (PPPP) test (0= no pain, 1= pain unilateraal, 2= pain bilateral), is positive when the bilateral sum score is ≥ 2 (0-2). For the longum dorsal sacro-iliacale ligament (LDL) test[27] (0= no pain, 1= complaint of pain without grimace, flinch, or withdrawal (mild), 2= pain plus grimace or flinch (moderate), 3= the examiner is not able to complete the test because of withdrawal (unbearable), the score is positive when the bilateral sum score bilateral is ≥ 2 (score range 0-6). The load transfer adduction test (score best to worse > 129-0 Newton) and abduction (score best to worse > 196-0 Newton)[50] is measured with a Microfet in Newtons.

The choice to include these specific variables in the analyses as potential prognostic factors is based on a literature review[30], the quality of tests, and clinical experience in the SJC.

Outcomes

Outcomes are assessed at intake, at the start and end of therapy, and at 5 and 12 months after start of therapy using questionnaires (Figure 1). An international group of back pain researchers recommended a standard battery of outcome measures to represent the multiple dimensions of outcome in the field of back pain.[14,16] We measured improvement of the patient with various measures: 1) pain intensity measured with a visual analogue scale (VAS; at the moment, minimum and maximum)[51,52], 2) low-back-pain-specific disability is measured with the Quebec Back Pain Disability Scale (QBPDS)[53], 3) generic health status. The Short Form (SF-36) is measured at start of therapy.[54-58] The three instruments have shown to be reliable, valid and responsive for a minimal important change (MIC).[32-35,51,53,59-64] 4) Global Perceived Effect (GPE) of the patient is measured with a 5-point scale (1= much improved, 2= slightly improved, 3= no change, 4= slightly worsened, 5= much worsened).[16] The GPE is proven valid[16,65], and 5) work participation. Work participation is measured by dividing 'current work hours' by 'former work employment hours' prior to CNLBP. No psychometric values are known for this instrument.

Analyses

Baseline characteristics of the patients are presented as descriptive statistics. Data on the course of CNLPB recovery during treatment are presented in graphs and tables at 5 and 12 months after start of therapy. The development of a multivariate prognostic model is based on principles and methods described by Moons and Altman et al..[66-69] The relationship between potential prognostic factors and outcome is evaluated using bivariate and multivariate analyses. For all outcome measurements, separate analyses are conducted to investigate prognostic factors at 5 and 12 months after start of therapy. Differences between baseline and follow-up scores are analysed using repeated measures analysis of variance. Logistic regression is used to determine odds ratios (ORs) of recovery, initially for each variable independently and then in a multiple regression model.

Recovery is operationalised into two definitions: 'improvement in'[16,33,70] and 'absolute'[16,71-73] recovery for each outcome measurement. All analyses are conducted with SPSS for Windows (version 18.0).

Results

Baseline measurements

A total of 2,545 patients [mean age 40.4 (10.9) years; 73.3% women] visited the SJC for an intake consultation between January 2003 and December 2008.
Of these, 1,760 patients [mean age 40.1 (10.6) years; 74.3% women] with CNLBP met the inclusion criteria, completed the 2-month therapy program, and were followed up at 5 and 12 months after start of therapy. Of this latter group, 96 followed the 'once a week' therapy program (with a duration of 4 months). A total of 785 patients [mean age 41.3 (11.5) years; 70.3% women] had the intake consultation but decided not to start therapy: reasons given for this included, only wanting the consultation and/or a diagnosis and/or some advice, referred to another specialist (e.g., psychologist, orthopaedic surgeon), decided not to come, travel distance too far, and unknown reasons.

The distribution of prognostic factors were similar in both the excluded and included groups regarding demographic characteristics, clinical status, psychological status, work-related parameters, and physical examination. Table 1 presents the baseline characteristics of the 1,760 patients; 74.3% is female with a (mean) duration of LBP complaints of 7.8 (SD 8.8) years. Of all patients, 90.2% had stable or increased low back pain intensity in the 3 months prior to intake. Pain intensity and disability showed moderate to severely impaired patients; 43.9% worked less because of their complaints. Of the 1,760 patients, 1,696 (96.4%) completed the 2-month therapy program, 1,564 (88.9%) participated in the 5-month follow-up and 965 (54.8%) completed the 12-month follow-up after start of therapy.

Table 1. *Baseline characteristics of the study population (n=1,760)*[a]

Variables	Population (n=1,760)	Missing value
Number of female participants	1,307(74.3)	0
Age in years: M (SD)	40.1(10.6)	0
Weight (kg): M (SD)*	75.3(14.8)	81(4.6)
Height (cm): M (SD)*	172.2(8.8)	70(4.0)
Demographic factors		
Low education*	716(40.7)	71(4.0)
Marital status/living with one adult*	1,515(86.1)	46(2.6)
Lifestyle		
Alcohol consumers; more than 2 per day*	73(4.1)	326(18.5)
Smoking 'yes'*	413(23.5)	326(18.5)
No drug consumers*	1,399(79.5)	313(17.8)
Clinical status		
Patients with BMI > 25*	783(44.5)	88(5.0)
Duration of complaints in years: M (SD)	7.7(8.8)	0
1 gradual emergence of NLBP	1,167(66.3)	30(1.7)
2 sudden emergence of NLBP	563(32.0)	
Cause		23(1.3)
1 accident/wrong movement	374(21.3)	
2 after physical overload	73(4.1)	
3 during pregnancy or after delivery	586(33.3)	
4 surgery pelvis/back or after HNP	32(1.8)	
5 unknown	672(38.2)	
Previous revalidation program*	186(10.6)	101(5.7)
Comorbidity	275(15.6)	88(5.0)
VAS Pain intensity LBP in mm: M (SD)		
1 present pain intensity	55.5(23.0)	5(0.3)
2 minimal pain intensity	34.6(21.7)	13(0.7)
3 maximal pain intensity	80.0(16.2)	13(0.7)
Pain intensity due to CNLBP in the previous 3 months		52(3.0)
1 stable pain intensity	865(49.1)	
2 increased pain intensity	723(41.1)	
3 decreased pain intensity	120(6.8)	
VAS degree of fatigue LBP in mm: M (SD)		
1 present fatigue	56.5(26.6)	118(6.7)
2 minimal fatigue	32.2(23.3)	169(9.6)
3 maximal fatigue	77.8(20.4)	169(9.6)
Disability (QBPDS): M (SD)	51.7(15.6)	8(0.5)
Psychological factors		
Fear avoidance (TSK): M (SD)	36.7(7.3)	50(2.8)
SF-36 (health-related quality of life)		
PCS	31.8(7.1)	493(28.0)
MCS	46.5(10.3)	493(28.0)

Variables	Population (n=1,760)	Missing value
Work-related factors		
Employment status benefit	924(52.5)	353(20.1)
Work participation		161(9.1)
1 100% working	391(22.2)	
2 1-99% working	488(27.7)	
3 not working	689(39.1)	
4 retired	31(1.8)	
Less work due to		460(26.1)
1 complaints	772(43.9)	
2 unemployed	19(1.1)	
3 different reasons	177(10.1)	
4 fully working	332(18.9)	
Physical examination		
LDL positive		
1 left	1,373(78.0)	29(1.6)
2 right	1,336(75.9)	31(1.8)
Mobility (VR) (degrees in flexion): M (SD)		
1 pelvis in flexion	40.7(15.7)	154(8.8)
2 low back in flexion	47.3(14.3)	154(8.8)
3 pelvis+low back in flexion (ROM)	88.0(24.6)	154(8.8)
ASLR positive (sum score ≥ 3)		
1 by general practitioner	1,442(81.9)	16(0.9)
2 by patient	1,217(69.1)	8(0.5)
ADL function – duration > 31 min without pain increase		
1 walking	410(23.3)	10(0.6)
2 cycling	312(17.8)	287(16.3)
3 sitting	432(24.5)	13(0.7)
4 lying	1,017(57.8)	15(0.9)
5 standing	106(6.1)	9(0.5)
PPPP positive (uni or bilateral)	1,110(63.1)	50(2.8)
Load transfer Abduction (Newton): M (SD)	224.9 (96.4)	137 (7.8)
Load transfer Adduction (Newton): M (SD)	172.5 (87.2)	136 (7.7)
B200 Isostation (strength) (Newton): M (SD)		
1 extension	81.6(45.8)	107(6.1)
2 flexion	65.2(45.0)	106(6.0)
3 lateroflexion left	68.1(41.2)	106(6.0)
4 lateroflexion right	74.2(39.4)	106(6.0)
5 rotation left	34.6(23.1)	107(6.1)
6 rotation right	33.4(22.5)	108 (6.1)

Values are numbers (percentages) unless stated otherwise.

[a] these factors were reported when therapy started, or gathered from the personal status; M = mean; SD = standard deviation; BMI = Body Mass Index; NLBP = non-specific low back pain; VAS = Visual analogue scale; QBPDS = Quebec Back Pain Disability Scale; TSK = Tampa Scale Kinesiophobia ;SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary; SCL-90 = Symptom Checklist; GPE = Global Perceived Effect; ADL= activities of daily living; VR = video registration; ASLR = Active Straight Leg Raise; PPPP = Posterior Pelvic Pain Provocation test; LDL = long dorsal sacro-iliac ligament.*

Discussion

Little information is available on the prognostic factors for recovery in patients with chronic non-specific low back pain. The present study is designed to provide insight into the course and prognostic factors for recovery in patients with CNLBP who are managed in a rehabilitation centre.

The study population was recruited from a multidisciplinary outpatient rehabilitation clinic (part of regular care), which leads to a more pragmatic approach regarding the prognosis of patients with CNLBP. In the 6 years during which patients have been followed for 12 months after start of therapy, the procedure of data recording and the follow-up period has been consistent. This limits information bias for the outcome recovery. Another strength of this study is that use of five domains of recovery allows to describe and analyse a broader perspective of relevant health outcomes for patients with CNLBP.

The study also has some limitations. First, we are unable to present the natural (untreated) course of CNLBP, because all patients receive multidisciplinary treatment during rehabilitation.[74,75] Also, most changes in outcome measurements are reported by the patients themselves, which might lead to some bias. The existing SJC procedure was maintained with regard to the follow-up. This probably decreased the response rate (especially at 12 months after start of therapy) because some patients were no longer motivated or were not approached to provide a response if they did not respond to the postal requests.

Impact of this study

This study provides information on relevant prognostic factors for recovery, and presents data on the course of patients with CNLBP following a multidisciplinary rehabilitation program.

Authors' contributions

All authors participated in the design of the study. KV drafted the manuscript with input from the other authors. All authors read, revised and approved the final manuscript.

Competing interests

The author(s) declare that they have no competing interests.

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CHAPTER 4

Prognosis and course of pain in patients with chronic non-specific low back pain: a 1-year follow-up cohort study

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under revision

Abstract

Background. It remains unclear to what extent patients recover from chronic non-specific low back pain (NSLBP). The study objectives were to determine a) the course of CNLBP in tertiary care and b) which factors predicted 5 and 12 month outcomes.

Methods. This prospective study includes 1,760 CNLBP patients from a rehabilitation clinic (mean age 40.1 years, SD 10.6). After baseline measurement patients followed a 2-month multidisciplinary therapy program; evaluation took place at 2, 5 and 12-months post-baseline. Recovery was defined as: 1) relative recovery (30% improvement on the pain, Visual Analogue Scale (VAS) compared to baseline), and 2) absolute recovery (VAS pain ≤ 10 mm). The multivariate logistic regression analysis included 23 baseline characteristics.

Results. Patient-reported intensity of back pain decreased from 55.5 (SD 23.0) at baseline to 37.0 (SD 23.8), 35.3 (SD 26.1) and 32.3 (SD 26.9) at 2, 5 and 12-months follow-up, respectively. Younger age, back pain at baseline, no psychological/

physical dysfunction (Symptom Check List-90, item 9) and higher baseline scores on the physical (PCS) and mental component scale (MCS) of quality of life (Short Form-36) were positively associated with recovery at 5 and 12 months. At 5-months follow-up, higher work participation at baseline was also a prognostic factor for both definitions of recovery. At 12-months follow-up, having comorbidity was predictive for both definitions.

Conclusion. The results of this study indicate that in CNLBP patients bio-psycho-social prognostic factors may be important for clinicians when predicting recovery in back pain intensity during a 1-year period.

Keywords. chronic non-specific low back pain; course; prognosis; cohort study; logistic regression

Introduction

A recent study in the Lancet[1] reported that low back pain stands out as the leading musculoskeletal disorder because of a combination of similarly high prevalence and a greater disability weight associated with this health state. Low back pain was one of the four most common disorders in all regions, and was the leading cause of years lived with disabilities (YLDs) in all developed countries. Low back and neck pain accounted for 70% of all YLDs from musculoskeletal disorders, and for every YLD due to neck pain there were 2.5 YLDs related to low back pain. The burden as estimated in this study is substantially higher than previously assessed 20 years ago. Across all countries surveyed, respondents consistently recorded high levels of health loss caused by pain. These findings combined with the 33.3% increase in YLDs from 1990 to 2010 driven largely by population growth and ageing have important implications for health systems.

Non-specific low back pain (NSLBP) is defined as pain and discomfort, localised below the costal margin and above the inferior gluteal folds, with or without leg. pain.[2,3] Because this pain often leads to medical consultations and/or sick leave, there is considerable medical and socioeconomic impact on the individual, family and society.[2,3] In the Netherlands, about 40-50% of the population experiences low back pain during a 12-month period. Also, about one-fifth of the adult population has reported CNLBP, i.e. symptoms present for ≥ 3 months[4], and about 14% of the Registered disabled is incapacitated due to spine-related disorders.[4] Therefore, the economic burden of CNLBP is particularly high and is compounded by the psychological burden on patients. Given the high prevalence, it is important to study risk factors for development, as well as the course of CNLBP and factors that influence its prognosis. Such information is important for patient education/management and to develop interventions for CNLBP, especially if modifiable prognostic factors are identified. However, few data are available on the clinical course of CNLBP and the prognostic factors related to outcomes at follow-up.[5]

Therefore, this prospective cohort study aims to 1) describe the course of back pain intensity in patients with CNLBP after receiving multidisciplinary therapy, and 2) develop a prognostic model predicting recovery in these patients at 5- and 12-months follow-up.

Methods

Study design and population

Patients were recruited (January 2003-December 2008) in a multidisciplinary outpatient rehabilitation clinic the 'Spine & Joint Centre' (SJC) in Rotterdam, the Netherlands. Patients were evaluated by means of physical examinations and/or questionnaires at baseline and at 2, 5- months at the location SJC and postal at 12-months follow-up. The Medical Ethics Committee of SJC approved the study protocol and all patients provided informed consent. Details on the study design of this prospective cohort study and intervention are published elsewhere.[6]

Patients with CNLBP, not recovering after primary and/or secondary care were referred by their general practitioner (GP) or specialist to the SJC for a diagnostic consultation. Inclusion criteria for this study were: 1) men and women aged ≥ 18 years; 2) with CNLBP (i.e., duration of low back pain for ≥ 3 months); 3) previous and insufficient treatment in primary and/or secondary care (e.g., physiotherapy); and 4) signed informed consent. Exclusion criteria were insufficient knowledge of the Dutch language; signs indicating radiculopathy, asymmetric Achilles tendon reflex and/or (passive) straight leg raise test restricted by pain in the lower leg; positive magnetic resonance imaging findings for disc herniation; recent (< 6 months) fracture, neoplasm or recent previous surgery (< 6 months) of the lumbar spine, the pelvic girdle, the hip joint, or the femur; specific causes such ankylosing spondylitis and systemic disease of the locomotor system; and being pregnant or ≤ 6 months post-partum at the moment of consultation.

Outcome measures and defining recovery

The outcome pain intensity is one of the 5 outcomes (back pain intensity, disability due back pain, work participation, quality of life and patients' perceived recovery) measured in this prospective cohort study. The choice for the outcome pain intensity is because this is important to the patient and also the most published outcome measurement in prognostic studies,[7] but the main objective of the rehabilitation program is normal behaviour of movements.[8,9] To determine the course of back pain intensity in patients with CNLBP, the Visual Analogue Scale (VAS) was used (range 0 mm=no back pain to 100 mm=unbearable back pain). Recovery was defined in two ways based on a minimally clinical important change (MCIC) in low back pain (LBP) as described by Ostelo et al.[10] and Helmhout et al.[11] for intensity of LBP.

First, 'relative recovery'' was defined as a 30% or more improvement compared to baseline (considered a clinically relevant difference) on the VAS back pain at follow-up measurements.[10,12] Second, 'absolute recovery' was defined as a VAS score of ≤ 10 mm at follow-up measurement.

Potential prognostic factors

Initially, 47 prognostic factors were considered relevant for inclusion in the analyses. However, to comply with the rule of at least 10 events per variable in the analysis, we had to restrict the number of potential prognostic factors.[13] The choice for eligible factors was made using the policy Delphi procedure in which the factors were independently scored (on a 4-point Likert scale ranging from 1=very important to 4=not important) by 8 experts.[5,14,15] The panel has experience in patients with CNLBP by research and/or working in the field, we consider them as experts. There were 3 rounds and each time the responses were aggregated, tabulated, summarized, and returned to the experts. In the third round the experts were asked to decide whether to keep or remove the factor from the list, through consensus meeting. The final list of consisted of 23 potential factors that were included by at least 80% consensus.[9] The following continuous variables (measured at baseline) were used in the analysis: age, duration of back pain in years, present back pain intensity (VAS: 0-100 mm), degree of present fatigue (VAS 0-100 mm), Quebec Back Pain Disability Scale (QBPDS: 0-100), Tampa Scale for Kinesiophobia (TSK, 17-68), Short-Form Health survey 36 [SF-36, Physical Component Scale (PCS) and Mental Component Scale (MCS)], Symptom Checklist 90 (SCL-90; item 9; psychoneurosis), work participation (0-100%), and the B200 Isostation (strength of back extension in Newton). The following categorical variables (split into ≥ 2 categorical variables) were included: body mass index (BMI; ≤ 24.9, 25-29.9, ≥ 30 kg/m^2), cause of back pain (accident movement; after physical load; during pregnancy or after delivery; unknown; surgery pelvis/back or herniated nucleus pulposus), pain in the previous 3 months (stable; increased; decreased), and the duration of walking, sitting, standing (0-15, 16-30, 31-60, 61 min) during daily activities. Dichotomized variables were: gender, comorbidity (none vs. having one of more comorbidity), level of education (< high school vs. ≥ high school/university), married/living with one adult (yes/no), previous rehabilitation treatment (no vs. one or more previous rehabilitation treatment) and employment status benefit (no vs. different types of government welfare benefits). For the excluded factors we refer to Verkerk et al..[9]

Treatment at the Spine & Joint Centre

The multidisciplinary treatment at the SJC centre used a bio-psychosocial approach consisting of 16 sessions of 3 h each during a 2-month period (total of 48 h). Patients were coached by a multidisciplinary team (e.g., a physical therapist, physician, health scientist, psychologist).[6]

After this 2-month period, patients are encouraged to continue the training program independently for at least 3 months, twice a week, in a local, regular health center located near their home environment.

Data analysis

Course of pain

Descriptive statistics were used to describe the patients course of back pain intensity at baseline, and at 2, 5 and 12-months follow-up. The percentage of patients with CNLBP defined as recovered based on a 30% improvement of the back pain intensity and absolute recovered (VAS pain ≤ 10 mm) at 2, 5 and 12 months follow-up was calculated.

Model development

Data from all patients with CNLBP receiving a multidisciplinary treatment were used to develop a prognostic model for back pain intensity recovery at 5 and 12 months.

Step 1. Using a correlation matrix, eligible prognostic factors were identified which were highly correlated ($r > 0.8$). This was the case for the B200 Isostation (strength in flexion, extension, lateroflexion, rotation) and the SCL-90 (item 1-8). Only the B200 extension and the total score item 9 of the SCL-90 were included in the analysis.[16]

Step 2. The continuous factors were checked for linearity using spline regression curves; this revealed a non-linear relationship between BMI and the score on VAS pain for back pain. Therefore, BMI was changed into a categorical variable.[17]

Step 3. Imputation of missing values in the data was carried out by multiple imputations. A total of 5 imputed datasets were used.[17-19] To develop our prognostic model a multivariable logistic regression analysis was performed.[16,20-22] Results of 5 imputed datasets were compared when 40 imputated datasets are used to see if the results would change; this number was used because in the initial model selection about 40% of the patients at 12 months was missing. Because the results were similar, 5 imputed datasets were used as primary analysis method. We also compared the results with complete case analysis (CCA), i.e. all patients with missing data were excluded from the analyses.[16,18,19]

Step 4. The most important prognostic variables were selected using a multivariable logistic regression analysis (stepwise method, backward likelihood ratio $p < 0.157$).[16,23] The selection of variables was performed over all the imputed datasets using Rubin's rules.[24] To assess whether the level of significance influenced the final prognostic model for all models, the selection of variables was repeated with p-values of 0.05 and 0.157.

Step 5. A sensitivity analysis was also performed using VAS cut-off values of ≤ 20 mm for absolute recovery and the same p-values.[12,25,26]

Missing data and the impact of nonresponders at baseline and 12 months follow-up was analysed by comparing patients' with response status, using summary measures. All analyses were done using SPSS version 18.0 (SPSS Inc., USA) and R software (R Foundation for Statistical Computing, Vienna, Austria).

Performance of the prognostic model

We checked the performance of the model with regard to the goodness of fit (Hosmer-Lemeshow test), the explained variation, and the discriminative ability of the model. The explained variation is the extent to which the outcome can be predicted by (the predictors in) the model in current dataset(s). The discriminative ability is reflected by the area under the receiver operating characteristics curve (AUC). The AUC represents the ability of the prognostic model to identify the patient who will recover from back pain intensity in two patients with different outcomes, and ranges from 0.5 (chance) to 1.0 (perfect discrimination).[27] Bootstrapping techniques were used to internally validate our models, i.e. to simulate the performance with respect to the explained variance and the AUC in comparable patient datasets.[21,22,28,29]

All analyses were done with SPSS version 18.0 (SPSS Inc., USA) and R software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Population

A total of 1,760 patients [mean age 40.1 (10.6) years; 74.3% women] with CNLBP participated in the study. Of these, 1,695 (96.3%) completed the 2-month multidisciplinary treatment, 1,564 (88.9%) completed the 5-months follow-up and 960 (54.5%) completed the 12-months follow-up. Table 1 presents the baseline characteristics of the 1,760 patients and the distribution of the possible prognostic factors . Responders at 12 months were likely to be female (77.0 vs 70.9%), married of living with one adult (90.2 vs 81.1%) and were more at work (53.1 vs 46.2%) than non responders (see appendix 1 for full details of baseline and 12 months follow-up). There were no reported differences between responders and non responders on the main outcomes.

Course of chronic low back pain

At baseline, the participants (n=1,760) reported a mean back pain intensity of 55.5 (SD 23.0) on the 0-100 mm VAS; at the end of therapy (n=1,695) this had decreased to a mean of 37 (SD 23.8). At 5 and 12-months follow-up the remaining patients reported a mean score of 35.3 (SD 26.1) and 32.3 (SD 26.9), respectively (Table 2).

Table 1. *Baseline characteristics of the study population (n=1,760)*[a]

Characteristic	Patients (n=1,760)
Number of female patients	1,307(74.3)
Age in years: M (SD)	40.1(10.6)
Demographic factors	
Low education	716(40.7)
Marital status/living with one adult	1,515(86.1)
Clinical status	
Patients with BMI > 25*	783(44.5)
Duration of complaints in years: M (SD)	7.7(8.8)
Cause reported by patient:	
1 accident/wrong movement	374(21.3)
2 after physical overload	73(4.1)
3 during pregnancy or after delivery	586(33.3)
4 surgery pelvis/back or after HNP	32(1.8)
5 unknown	672(38.2)
Previous revalidation program	186(10.6)
Comorbidity	275(15.6)
Pain intensity LBP (VAS in mm): M (SD)	
1 present pain intensity	55.5(23.0)
Pain intensity due to CNLBP in the previous 3 months	
1 stable pain intensity	865(49.1)
2 increased pain intensity	723(41.1)
3 decreased pain intensity	120(6.8)
Degree of fatigue LBP (VAS in mm): M (SD)	
1 present fatigue	56.5(26.6)
Disability (QBPDS): M (SD)	51.7(15.6)
Psychological factors	
Fear avoidance (TSK): M (SD)	36.7(7.3)
SCL90 item 9 M(SD)	149.3(39.7)
SF-36 (health-related quality of life)	
PCS	31.8(7.1)
MCS	46.5(10.3)
Work-related factors	
Employment status benefit	924(52.5)
Work participation	
1 100% working	391(22.2)
2 1-99% working	488(27.7)
3 not working	689(39.1)
4 retired	31(1.8)
Physical examination	
ADL function – duration > 31 min without pain increase	
1 walking	410(23.3)
2 sitting	432(24.5)
3 standing	106(6.1)
B200 Isostation (strength) (Newton): M (SD)	
1 extension	81.6(45.8)

Values are numbers (percentages) unless stated otherwise.

[a] *M = mean; SD = standard deviation; BMI = Body Mass Index; CNLBP = chronic non-specific low back pain; VAS = Visual analogue scale; QBPDS = Quebec Back Pain Disability Scale; TSK = Tampa Scale Kinesiophobia ; SCL-90 (item 9)= Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary; ADL= activities of daily living. Missing values ranged from 0.5% (n=9) to 28% (n=493).*

Compared with baseline, after 2 months therapy a 30% (or more) improvement on the VAS was reported by 904 patients (53.8%); at 5 and 12-months follow-up these data were 862 (55.2%) and 578 (60.5%) patients, respectively.

For absolute recovery from back pain, at baseline 66 patients (3.8%) had a score ≤10 on the VAS but were included in therapy for other outcomes, e.g. back pain disability, quality of life, or work participation.[6] After 2 months therapy, 233 patients (13.7%) scored ≤ 10 on the VAS; at 5 and 12-months these data were 310 (19.8%) and 275 (28.6%) patients, respectively.

Table 2. *Course of back pain intensity scores in patients with chronic non-specific low back pain at 2-, 5- and 12-months follow-up*

	Baseline (n=1,608, 1,405)	5 months (n=820)	5 months (n=820)	12 months (n=589)
Back pain intensity (VAS): mean (SD)	55.5 (SD 23.0)	37.0 (SD 23.8)	35.3 (SD 26.1)	32.3 (SD 26.9)
30% improvement in pain (VAS)		53.8%	55.2%	60.5%
		(904/1679)	(862/1561)	(578/955)
Absolute recovery on pain score (≤ 10 points on VAS)	3.8%	13.7%	19.8%	28.6%
	(66/1755)	(233/1695)	(310/1564)	(275/960)

VAS =Visual Analogue Scale; mean (SD= standard deviation), n=number of patients.

Relative recovery: prognostic models at 5 and 12-months follow-up

At 5-months follow-up, multivariate analyses resulted in a final model (AUC=0.66, 95% CI 0.64-0.69) which included 9 prognostic factors, together explaining 11% of the variation in outcome: younger age, female gender, a higher BMI > 25 kg/m^2 at baseline, no previous rehabilitation treatment, more back pain intensity at baseline, no psychological/physical dysfunction (psycho-neuroticism) as measured with the SCL-90 (item 9), higher scores on the SF-36 PCS and MCS at baseline, and higher work participation at baseline (Table 3). The prognostic factor most strongly associated with improvement was a BMI of ≥ 25-29.9 kg/m^2 (OR 1.27, 95% CI 0.99-1.62) and a higher work participation at baseline (OR 1.27, 95% CI 0.93-1.73).

At 12-months follow-up the final multivariate regression model (AUC=0.65, 95% CI 0.61-0.67) included 9 prognostic factors, together explaining 10% variation in outcome: younger age, female gender, being married/living with one adult, higher level of education, no comorbidity, more back pain intensity at baseline, higher strength at the extension direction with the B200 Isostation at baseline, no fear of movement at baseline, and higher scores on the PCS with the SF-36. Being married or living with one adult (OR 1.6, 95% CI 0.99-2.57) was the strongest prognostic factor associated with a 30% improvement in recovery (Table 3).

With regard to internal validation of the model, the explained variance was 11% and the AUC was 0.66 (95% CI 0.64-0.69) for the 5-month model, compared with 10% and 0.66 (95% CI 0.61-0.67), respectively, for the 12-month model.

Table 3. *Multivariable models of prognostic factors for 30% improvement in chronic non-specific low back pain, back pain intensity at 5- and 12-month follow-ups*

Variable	5-months follow-up			12-months follow-up		
	OR	95% CI	p-value	OR	95% CI	p-value
Age in years	0.98	0.97-0.99	< 0.001	0.98	0.96-0.99	0.03
Gender (male/ female)	0.80	0.62-1.03	0.09	0.72	0.49-1.07	0.10
Back pain intensity at baseline (VAS)	1.02	1.02-1.03	< 0.001	1.01	1.01-1.02	< 0.001
SF-36 PCS	1.05	1.03-1.08	< 0.001	1.04	1.02-1.06	< 0.001
Sf-36 MCS	1.02	0.99-1.04	0.07			
SCL-90 (item 9)	0.99	0.99-0.99	0.03			
BMI ≥ 25-29.9 kg/m^2	1.27	0.99-1.62	0.06			
BMI ≥ 30 kg/m^2	1.04	0.74-1.47	0.81			
Previous rehabilitation (yes/no)	0.68	0.50-0.94	0.02			
Work participation	1.27	0.93-1.73	0.13			
Education				1.30	0.93-1.82	0.11
Comorbidity (no/yes)				0.76	0.52-1.11	0.15
Married/being with one adult (yes/no)				1.60	0.99-2.57	0.05
B200 Isostation extension				1.00	0.99-1.01	0.13
TSK				0.97	0.95-0.99	0.02

95%-CI= 95% confidence interval, OR = odds ratio, an OR > 1 reflects a higher probability of 30% recovery for the outcome back pain intensity and an OR < 1 a lower probability of 30% recovery for the outcome back pain intensity, compared to the reference category. OR estimated after multiple imputation (n=5 datasets) with p-value of 0.157. VAS = Visual analogue scale; SCL-90 (item 9)= Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary. The variable BMI is a category value of 3 (18-24.9 kg/m^2; ≥ 25-29.9kg/m^2; ≥ 30kg/m^2)

Sensitivity analysis for relative recovery

For the 5-months follow-up, sensitivity analysis of the 30% improvement with p-values of 0.05 or 0.157, and using a CCA or 5 or 40 imputed datasets, yielded similar results on 6 of the 9 prognostic factors. Repeating the analyses at 12 months resulted in 5 of the 9 factors. Because (overall) similar predictors were included, this indicates that the most important prognostic factors were selected. In the various models, these sensitivity analyses showed an AUC of 0.64-0.68 at 5 and 12 months follow-up, with an explained variance of 8-11% that included 4-9 of the prognostic factors.

With regard to internal validation of the model, the explained variance was 10-11%. For all models, at 5 months the AUC was 0.66. At 12-months follow-up the explained variance was 8-11% and the AUC was 0.64-0.66 AUC (complete data can be obtained from the first author).

Absolute recovery: prognostic models at 5 and 12-months follow-up

The final multivariable model (AUC=0.69, 95% CI 0.66-0.72) for 5-months follow-up consisted of 6 prognostic factors, with an explained variance of 11% (Table 4): younger age, lower score on back pain at baseline, no psychological/physical dysfunction (psycho-neuroticism on SCL-90 (item 9), higher scores on the SF-36 PCS/MCS at baseline, and more work participation at baseline. Work participation (OR 1.34, 95% CI 0.93-1.93) was the strongest prognostic factor in the model associated with absolute recovery.

The final prognostic model for 12-months follow-up consisted of 8 factors: younger age, a higher BMI ≥ 30 kg/m^2 at baseline, no comorbidity, less back pain at baseline, higher scores on the SF-36 PCS and MCS at baseline, higher disability score at baseline, and having stable or more back pain intensity due to CNLBP in the previous 3 months. The strongest prognostic factors associated with absolute recovery were stable or more back pain intensity due to CNLBP in the previous 3 months (OR 1.42, 95% CI 1.02-1.99) and BMI ≥ 30 kg/m^2 (OR 1.74, 95% CI 1.10-2.76). The explained variance was 18% with an AUC of 0.73 (95% CI 0.71-0.76).

With regard to internal validation of the model, at 5-months the explained variance was 11% and the AUC was 0.69 (95% CI 0.66-0.72); at 12-months follow-up this was 18% and 0.73 (95% CI 0.71-0.76), respectively (i.e., after the start of therapy and before/after analysing the internal validation).

Table 4. *Multivariable models of prognostic factors for absolute recovery on chronic non-specific low back pain, back pain intensity (VAS ≤ 10 point) at 5- and 12-month follow-ups*

Variable	5-months follow-up			12-months follow-up		
	OR	95% CI	p-value	OR	95% CI	p-value
Age in years	0.97	0.96-0.99	< 0.001	0.97	0.95-0.99	0.03
Back pain intensity at baseline (VAS)	0.99	0.98-0.99	< 0.001	0.98	0.98-0.99	< 0.001
SF-36 PCS	1.05	1.03-1.07	< 0.001	1.07	1.03-1.11	0.00
SF-36 MCS	1.02	0.99-1.04	0.13	1.02	1.01-1.04	0.02
SCL90 (item 9)	0.99	0.99-1.00	0.09			
Work participation	1.34	0.93-1.93	0.11			
BMI ≥ 25-29.9 kg/m^2				1.25	0.84-1.87	0.25
BMI ≥ 30 kg/m^2				1.74	1.10-2.76	0.02
Co morbidity (yes/no)				0.65	0.42-1.02	0.06
Course of pain intensity due to CNLBP in the previous 3 months (increase of pain)				1.42	1.02-1.99	0.04
Course of pain intensity due to CNLBP in the previous 3 months (decrease of pain)				1.62	0.76-3.47	0.19
Disability at baseline (QBPDS)				1.01	1.01-1.02	0.08

95%-CI= 95% confidence interval, OR = odds ratio, an OR > 1 reflects a higher probability of 30% recovery for the outcome back pain intensity and an OR < 1 a lower probability of 30% recovery for the outcome back pain intensity, compared to the reference category. OR estimated after multiple imputation (n=5 datasets) with p-value of 0.157. CNLBP = chronic non-specific low back pain; VAS = Visual analogue scale; SCL-90 (item 9)= Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary. The variable BMI is a category value of 3 (18-24.9 kg/m^2; ≥ 25-29.9kg/m^2; ≥ 30kg/m^2). The variable Course of pain intensity due to CNLBP in the previous 3 months is a category value of 3 (0=stable, 1= increase of pain, 2=decrease of pain).

Sensitivity analysis for absolute recovery

Sensitivity analysis of the cut-off for the VAS ≤ 10 mm with p-values of 0.05 or 0.157 and/or 5 or 40 imputed datasets or CCA for the 5 and 12-months follow-up resulted in similar prognostic factors. In the various models, multivariate analyses showed an AUC of 0.68-0.76 for the 5 and 12-months follow-up that included 4-12 prognostic factors, together explaining 10-15% of the variation.

With regard to internal validation of the model, at 5-months the explained variance was 10-12% and the AUC was 0.68-0.69 for all models compared with 11-15% and 0.70-0.71 AUC at 12-months follow-up (complete data can be obtained from the first author).

Absolute recovery (VAS ≤ 20 mm) on back pain intensity

Repeating the analysis with a cut-off point of ≤ 20 for absolute recovery with p-values of 0.05 or 0.157 and/or 5 or 40 imputed datasets or CCA for the 5 and 12-months follow-up resulted in similar prognostic factors. These analyses had an AUC of 0.70-0.73 for the 5 and 12-months follow-up that included 6-9 prognostic factors with an explained variance of 15-20%.

For internal validation of the model, at 5 months the explained variance was 16% and the AUC was 0.70 for all models, compared with 20% and 0.73, respectively, for the 12-months follow-up (complete data can be obtained from the first author).

Discussion

The course a CNLBP after 2 months of cognitive behavior therapy shows a decline of back pain that continued up to 1-year follow-up. Back pain continued to decrease, albeit more slowly, between 5 and 12-months follow-up. The most important finding of this prospective cohort study is that there were similarities in prognostic factors between the two definitions of recovery (at least 30% improvement and VAS ≤ 10 mm) and also at the different moments of follow-up. Recovery at 5 and 12-months follow-up was associated with younger age, back pain intensity at baseline and higher baseline scores on the SF-36 PCS/MCS. For both definitions of recovery, at 5-months follow-up a higher work participation rate at baseline and no psychological/physical dysfunction (psycho-neuroticism) measured with the SCL-90 (item 9) were prognostic factors and at 12-months follow-up comorbidity was prognostic.

The reported decrease in back pain intensity over a 1-year period is similar to other studies performed in the general population, primary or tertiary care.[30-32] Our study also showed that direct after the 2-month multidisciplinary cognitive behaviour therapy at the rehabilitation centre SJC, the patients experienced the greatest change in improvement compared to the baseline in all outcomes compared to 5 and 12 month follow-up.

A similar pattern was reported in the first 4-6 weeks in a recent meta-analysis[33] and other studies[30,32,34] describing slowly advancing reductions in average pain and disability between 6 and 52 weeks. The duration of complaints in our study population was on average 7.7 years. Recent studies[35,36] reports that most patients with back pain appear to follow a particular pain trajectory over longer time periods. It can be that a particular pain trajectory will have certain clinical characteristics. This could influence which prognostic factor is important as also the effect of a rehabilitation program.[35]

Our systematic review on prognostic factors in CNLBP patients showed no association between age and sex at ≤ 6 months follow-up and smoking at ≥ 12 months follow-up.[5] Conflicting evidence was found at ≤ 6 months follow-up for fear of movement on back pain intensity; at ≥ 12 months follow-up conflicting evidence was found for the factors age, sex, work status and physical job demands and limited evidence for no association between the outcome back pain intensity and the factor social work.[5] The present results are not in accordance with this latter review, with the exception that fear of movement has no association with back pain intensity at 5 and 12-months follow-up. The reason for these differences could be due to the quality of the studies included in the systematic review, i.e. the risk of bias was high in most studies and their statistical performance poorly described.[5]

Recovery is a complex construct and although there is no consensus on how it should be defined or measured, there is consensus on which outcomes are relevant in the process of recovery.[12,25,37,38] A commonly used definition of a 'clinically meaningful improvement' on back pain intensity is 30% improvement on a VAS score compared to baseline (15-20 mm).[12,39] This definition gives clinicians and patients a useful threshold for identifying clinically meaningful improvement during a follow-up period or therapy process compared to natural fluctuations. However, apart from a 30% improvement, patients are also interested in prognostic factors to reach optimal/absolute recovery. The cut-off point on the VAS scale that classifies patients as 'absolutely' recovered is not yet known. The choice of outcome definition does make an important difference. Patients with severe back pain (high VAS score) at baseline are probably more likely to achieve a 30% change over time than to drop from a high baseline VAS score to a score of ≤ 10 mm. A systematic review by Kamper et al. described 3 studies that reported the complete absence of pain, whereas 3 other studies fixed a cut-off score on the instrument (e.g., VAS ≤ 10/100 mm; NRS ≤ 1/10).[40] CNLBP did not have a higher cut-off score for pain and disability than acute NSLBP.[25] Our study shows that the AUC and explained variance was higher for ≤ 20 mm than for ≤ 10 mm VAS, and 5 out of 6 factors were similar. However, selecting a higher cut-off will improve the sensitivity: i.e. a greater proportion of patients who consider themselves recovered, will be correctly classified.

Missing data for baseline assessment items ranged from 0.5-28%. At the 5 and 12-month evaluations, 10.8% and 45.5% of the patients, respectively, did not respond (mainly due to not returning the follow-up questionnaires).

We expect that our data are 'missing at random', which is not uncommon in prognostic studies with a relatively long follow-up period. We chose to impute missing data by using known variables of the patients[41]; the multiple imputation procedure is assumed to be more valid than deleting participations with missing data from the analyses. Not using the full study sample, but only patients with complete data, can reduce the model's validity.[17,29,41] Also, performing sensitivity analyses to compare the data with more imputated datasets (n=40 and n=5), level of p-values of 0.05 and 0.157 and CCA[16,19,27,29] showed little or no difference in the identified prognostic factors; this reduces the risk of bias. Finally, the chance of overfitting our models by including too many variables was avoided by using a 'rule of thumb' to calculate the maximum number of variables. Finally, fewer variables were included in the models than was possible.[24]

In the current study, the prognostic models have typically c-index between 0.6-0.85 (Royston et al., 2009) and normal confidence interval for the validation model.[22] The low explained variance (R^2) is higher than in other studies (Verkerk et al., 2012), but still recommending that other prognostic factors (e.g., physical parameters) may be of influence for the course of recovery.[6] A larger group of patients when using relative recovery will benefit from the treatment given and are correctly identified compared to absolute recovery. Choice of cuff-off point determines a lot. However, there are patients that may also improve from less intensive or another treatment. The generalizability of the results is somewhat limited because the patients were recruited from a rehabilitation centre for tertiary care and all had received multidisciplinary treatment. A strength of the current study is that data was collected prospectively from a cohort of patients in one daily clinical care centre, so the risk of confounding will be lower. Comparison these results with other settings (e.g. primary care or tertiary care) is the next step to tests the generalizability of the results. However, cognitive behaviour therapy with supervised exercises, educational and multi-disciplinary treatment, is one of the most common intervention for CNLBP in Dutch rehabilitation centres. Two Cochrane reviews[42,43] provided evidence of a greater improvement on the short term than other treatments. During the 5-month follow-up at SJC information was collected on adherence, 70% of the patients followed the therapy program at 5 months.

Better pain management coupled with identification and modification of patients' perception on back pain, being at work and their quality of life are clear targets for further research for interventions. More research is needed to clarify the course of patients with CNLBP and to establish whether our results are valid in other settings. A study in which patients complete a global perceived effect (GPE) which is then compared with back pain intensity (VAS) to determine when a patient experiences 'complete' recovery may provide more insight into the definition of 'absolute recovery'. The next step is external validation of the prognostic models to enable clinicians to eventually apply these models in daily practice.[17]

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Appendix 1. *Baseline characteristics of the study population with chronic non-specific low back pain*[a]

Characteristic	Patients (n=1,760)	Responders (n=965)	Non-responders (n=795)	Significance
Number of female patients	1,307(74.3)	743(77.0)	564(70.9)	.004*
Age in years: M (SD)	40.1(10.6)	40.6(10.7)	39.4 (10.4)	.252
Demographic factors				
Low education	716(40.7)	379(39.3)	337(42.4)	.085
Marital status/living with one adult	1,515(86.1)	870(90.2)	645(81.1)	.000*

Characteristic	Patients (n=1,760)	Responders (n=965)	Non-responders (n=795)	Significance
Clinical status				
Patients with BMI > 25*	783(44.5)	424(43.9)	359 (45.2)	.444
Duration of complaints in years: M (SD)	7.7(8.8)	7.7(8.9)	7.5(8.7)	.473
Cause reported by patient:				.912
1 accident/wrong movement	374(21.3)	201(20.8)	173(21.8)	
2 after physical overload	73(4.1)	42(4.4)	31(3.9)	
3 during pregnancy or after delivery	586(33.3)	330(34.2)	256(32.8)	
4 surgery pelvis/back or after HNP	32(1.8)	18(1.9)	14(1.8)	
5 unknown	672(38.2)	365(37.8)	307(38.6)	
Previous revalidation program	186(10.6)	103(10.7)	83(10.4)	.968
Comorbidity	275(15.6)	153(15.9)	122(15.3)	.723
Pain intensity LBP (VAS in mm): M (SD)				
1 present pain intensity	55.5(23.0)	54.5(22.8)	56.7(23.3)	.551
Pain intensity due to CNLBP in the previous 3 months				.206
1 stable pain intensity	865(49.1)	495(51.3)	370(46.5)	
2 increased pain intensity	723(41.1)	382(39.6)	341(42.9)	
3 decreased pain intensity	120(6.8)	68(7.0)	52(6.5)	
Degree of fatigue LBP (VAS in mm): M (SD)				
1 present fatigue	56.5(26.6)	54.8(26.6)	58.7(26.5)	.837
Disability (QBPDS): M (SD)	51.7(15.6)	50.4(15.1)	53.2(16.0)	.032*
Psychological factors				
Fear avoidance (TSK): M (SD)	36.7(7.3)	36.5(7.1)	36.9(7.6)	.105
SCL90 item 9 M(SD)	149.3(39.7)	145.2(36.1)	154.6(43.4)	.000*
SF-36 (health-related quality of life)				
PCS	31.8(7.1)	32.3(7.0)	31.3(7.3)	.505
MCS	46.5(10.3)	47.3(10.1)	45.6(10.4)	.462
Work-related factors				
Employment status benefit	924(52.5)	481(49.8)	443(55.7)	.059
Work participation				.019*
1 100% working	391(22.2)	222(23.0)	169(21.3)	
2 1-99% working	488(27.7)	290(30.1)	198(24.9)	
3 not working	689(39.1)	359(37.2)	342(43)	
4 retired	31(1.8)			
Physical examination				
ADL function – duration > 31 min without pain increase				
1 walking	410(23.3)	238(24.7)	168(21.2)	.440
2 sitting	432(24.5)	261(27.1)	164(20.6)	.042*
3 standing	103(5.8)	57(5.9)	46(5.8)	.291
B200 Isostation (strength) (Newton): M (SD)				
1 extension	81.6(45.8)	81.2(42.1)	82.1(50.1)	.000*

[a] *M= Mean; SD= standard deviation; LBP = low back pain; CNLBP = chronic non-specific low back pain; VAS = Visual analogue scale; SCL-90 (item 9)= Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary. The variable BMI is a category value of 3 (18-24.9 kg/m²; ≥ 25-29.9kg/m²; ≥ 30kg/m²). The variable Course of pain intensity due to CNLBP in the previous 3 months is a category value of 3 (0=stable, 1= increase of pain, 2=decrease of pain); ADL=Activities in Daily Life.*

CHAPTER 5

Prognosis and course of disability in patients with chronic non-specific low back pain: a 5 and 12-months follow-up cohort study

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Abstract

Background. Few data are available on the course of and predictors for disability in patients with chronic non-specific low back pain (CNLBP).
Objective. The purpose of this study was to describe the course of disability and identify clinically important prognostic factors of low-back-pain-specific disability in CNLBP patients receiving multidisciplinary therapy.
Study Design. A prospective cohort study was conducted.
Methods. A total of 1,760 patients with CNLBP who received multidisciplinary therapy were evaluated for their course of disability and prognostic factors at baseline and at 2, 5- and 12-months follow-ups. Recovery was defined as a 30% reduction in low-back-pain-specific disability at follow-up compared to baseline and as absolute recovery if the score on the Quebec Back Pain Disability Scale (QBPDS)

was ≤ 20 points at follow-up. Potential prognostic factors were identified using multivariable logistic regression analysis.

Results. Mean patient-reported disability scores on the QBPDS ranged from 51.7 (SD=15.6) at baseline to 31.7 (SD= 15.2), 31.1 (SD 18.2), and 29.1 (SD= 20.0) at 2, 5, and 12-months, respectively. The prognostic factors identified for recovery at 5 and 12-months were younger age and high scores on disability and on the 36=Item Short-Form Health Survey (SF-36) (Physical and Mental Component Summaries) at baseline. In addition, at 5-months follow-up, a shorter duration of complaints was a positive predictor, and having no comorbidity and less pain at baseline were additional predictors at 12-months follow-up.

Limitations. Missing values at 5- and 12-months follow-ups were 11.1% and 45.2%, respectively.

Conclusion. After multidisciplinary treatment, the course of disability in patients with CNSPBP continued to decline over a 12-month period. At 5- and 12-months follow-ups prognostic factors were identified for a clinically relevant decrease in disability scores on the QBPDS.

Keywords. chronic low back pain; prognosis; outcome assessment; disability, cohort

Introduction

There is no strong evidence to support the claim that 80 to 90% of low back pain (LBP) patients become pain free within 1 month; on average, 62% (range=42%-75%) of the patients still experienced back pain after 12 months.[1] Studies following patients over a 12-month period have shown that LBP is characterized as having periodic attacks and temporary remissions, rather than being "chronic".[1-3] Shorter periods of temporary remissions are frequently seen in patients with chronic nonspecific low back (CNLBP) (≥ 12 weeks) in combination with higher levels of limitations in activities.[4] A recent meta-analysis[5] reported that patients with acute, subacute (< 12 weeks), and persistent (> 12 weeks to 12 months) LBP experienced substantial reductions in pain and improvement in disability in the first 6 weeks, but only very small reductions in average pain and disability between 6 and 52 weeks were demonstrated. The course of limitations in activities among patients with CNLBP varies per patient.[4,6] Therefore, knowledge on the course and prognostic factors of disability experienced by patients with CNLBP might be clinically relevant for optimizing rehabilitation. The rehabilitation of normal patterns or activities of movements in patients with CNLBP is a focus during multidisciplinary treatment.[7]

A systematic review[8] including patients experiencing LBP for less than 8 weeks identified risk factors for developing persistent, disabling LBP. Prognostic factors for the development of persistent LBP at 1-year follow-up were high maladaptive

pain coping behaviours, presence of nonorganic signs, high baseline functional impairment, low general health status and presence of psychiatric comorbidities. Low levels of fear avoidance and low baseline functional impairment were the most useful items for predicting recovery at 1 year. Our recent systematic review on prognostic factors in patients with CNLBP (≥ 12 weeks) showed that, at short-term follow-up (≥ 6 months), there was no association between age and sex on disability and that, at long-term follow-up (≥ 12 months), there was no association among smoking, pain intensity, and fear of movement. Conflicting evidence was found at short-term follow-up for an effect of fear of movement on disability, and at long-term follow-up for the factors of age, sex, work status, physical job demands, sick leave and feelings of depression. Also, there was limited evidence for no association between the outcome disability and the factors leg. pain level and mobility. However, the methodological quality of the included studies was mostly poor (high risk of bias).[9]

Thus, overall, there is no strong evidence for associations that can help clinicians in their clinical decision-making to influence modifiable prognostic factors that might have a positive effect on disability. Therefore, the aims of this study were: (1) to describe the course of disability in patients with CNLBP (receiving multidisciplinary therapy) at 2-, 5- and 12-months follow-ups and (2) to identify prognostic factors of LBP-specific disability at 5 and 12 months after completing a multidisciplinary therapy program.

Method

Study design and participations

Patients were recruited (January 2003-December 2008) at the Spine & Joint Centre (SJC), a multidisciplinary outpatient rehabilitation clinic in Rotterdam, the Netherlands. All patients provided informed consent. Detailed information on the study design has been published elsewhere.[7] Participants were evaluated using mailed questionnaires and physical examinations at baseline and at 2, 5 and 12-months.

Therapy program

The multidisciplinary treatment at the SJC used a biopsychosocial approach to stimulate patients to adopt adequate (movement) behavior aimed at physical and functional recovery. Patients with CNLBP not recovering after primary or secondary care were referred by their general practitioner (GP) or specialist to the SJC for a diagnostic consultation. Diagnostic consultation consisted of a 3-hour intake session in which the patient completed several questionnaires and undertook history taking and a physical examination.

The physician could request an additional consultation with a psychologist or manual physiotherapist before deciding on treatment management. When patients were eligible for treatment, they were invited to participate in the study and informed consent was obtained. In the present study, LBP was defined as ''nonspecific'' (i.e., without a specified physical cause, such as nerve root compression, trauma, infection or the presence of a tumour). Pain in the lumbosacral region is the most common symptom in patients with nonspecific LBP. Pain may also radiate to the gluteal region or to the thighs, or to both.[10] Patients with CNLBP (complaints lasting ≥ 3 months) and not improving in primary care (mono-disciplinary) with the influence of psychological and social factors besides the physical factors on their complaints were invited to participate in the multidisciplinary treatment program. Those not eligible or not wanting to participate in this study were referred back to their GP.[7]

The sample in the current study consisted of a survival cohort with the following inclusion criteria: (1) men and women aged 18 years and over, (2) having CNLBP (defined as LBP with a duration of ≥ 3 months; 3), (3) previous and unsuccessful treatment in primary or secondary care (e.g., physical therapy), and (4) signed informed consent.

Exclusion criteria were: (1) insufficient knowledge of the Dutch language; (2) signs indicating radiculopathy, asymmetric Achilles tendon reflex, or passive straight leg raise test restricted by pain in the lower leg.; (3) positive magnetic resonance imaging findings for disc herniation; (4) recent (< 6 months) fracture or neoplasm or recent previous surgery (< 6 months) of the lumbar spine, the pelvic girdle, the hip joint, or the femur; (5) specific causes such ankylosing spondylitis and systemic disease of the locomotor system; and (6) being pregnant or ≤ 6 months post-partum at the moment of consultation.

The therapy program consisted of 16 sessions of 3 hours each during a 2-month period (a total of 48 hours) coached by a multidisciplinary team (physical therapist, physician, health scientist, and psychologist). Behavioral principles were applied to encourage patients to adopt adequate normal behavioral movement aimed at physical recovery. The Quebec Back Pain Disability Scale (QBPDS) was measured to indicate the limitations in activity.[7]

Five months after the start of the therapy program (2 months at the SJC + 3 months self-supporting activity), the patients were measured at the 5-month follow-up at the SJC. At 12-months follow-up, the measurement was performed by means of questionnaires mailed to the patients.

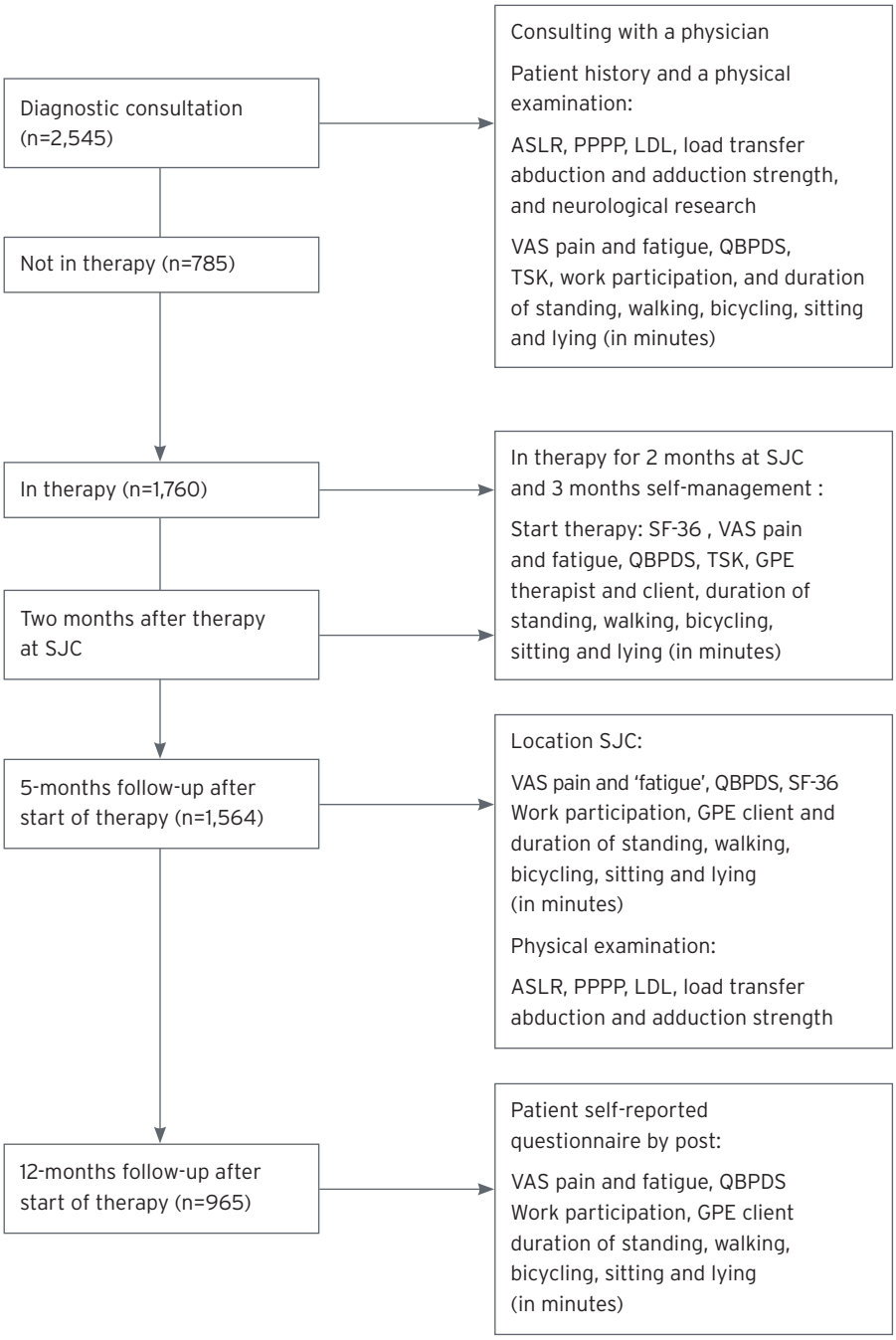

Figure 1. *Flow chart of the study design*

ASLR= Active Straight Leg Raise test, PPPP= Posterior Pelvic Pain Provocation test, LDL= longum dorsal sacroiliac ligament, VAS= Visual Analogue Scale, QBPDS= Quebec Back Pain Disability Scale, SF-36=Short Form, TSK= Tampa Scale for Kinesiophobia, GPE=Global perceived effect, SJC= Spine & Joint Centre

Outcome criteria

Outcome criteria were based on a minimally important change in LBP as described by Ostelo and collegeues[11,12] and Helmhout et al.[13] for LBP disability. The QBPDS is a 20-item self-administered instrument designed to assess the level of functional disability in patients with back pain (score range= 0-100). Higher scores indicate more disability. The QBPDS has shown to be reliable, valid and responsive measure.[14] The QBPDS was completed by the patients; therefore, the scores were not blinded for putative prognostic factors. Recovery from disability was operationalized into 2 definitions: (1) 30% improvement in recovery compared to baseline[11,12] (the QBPDS scores [0-100] were dichotomized into "no improvement in disability" and "improvement in disability," using a reduction of 30% at follow-up compared with baseline as a clinically relevant difference,[11-13]) and (2) "absolute recovery", which was defined as a QBPDS score of ≤ 20 points at follow-up.[11,15-17]

Prognostic factors

The baseline values of 47 prognostic factors were included in the analyses as important or potential prognostic factors. To comply with the rule of at least 10 events per variable in the analysis (which avoids incorrect estimation of variables), we had to restrict the total number of potential prognostic factors.[18] The choice for eligible factors was made: (1) using a policy Delphi procedure in which the factors were independently scored (on a 4-point Likert scale ranging from 1=very important to 4=not important) by 8 experts[9,19,20], and (2) based on the results of a systematic review on prognostic factors for recovery.[9,19,20] On the basis of the experts' opinions and the systematic review, 23 potential prognostic factors were included (Table 1).

The continuous variables were: age, duration of back pain in years, present pain intensity (visual analog scale [VAS]: 0-100 mm), degree of present fatigue (VAS: 0-100 mm), QBPDS score (range=0-100), Tampa Scale for Kinesiophobia (TSK) score (range=17-68), 36-Item Short-Form Health Survey (SF-36, Physical Component Summary [PCS] and Mental Component Scale [MCS]), Symptom Checklist-90 (SCL-90; item 9; psychoneurosis) score, B200 Isostation (Isotechnologies, Hillsborough, North Carolina) (back extension strength in Newtons) and work participation (0%-100%). Work participation was measured by dividing current work hours by former work employment hours prior to CNLBP. Some of patients were on partial sick leave due to back pain. Patients who were retired, not seeking work, unemployed as they have family care responsibilities gave no information.

The categorical variables were: body mass index (BMI: ≤ 24.9, 25-29.9, ≥ 30 kg/m^2), cause of back pain (accident or wrong move made by the patient, after physical load, during pregnancy or after delivery, unknown, pelvis or back surgery or Herniated Nucleus Pulposus); course of pain in the previous 3 months (stable, increased, decreased); and the duration of walking, sitting, and standing (0-15, 16-30, 31-60, > 61 minutes) during daily activities.

The dichotomized variables were: sex, comorbidity (none versus having one or more comorbidities), level of education (less than high school versus high school/ university), married or living with one adult (yes/no), previous rehabilitation treatment (none versus one or more previous rehabilitation treatments), and employment status benefit (none versus different types of government welfare benefits).

We excluded the following factors: weight, height, alcohol consumption, smoking, drug consumption, patient's gradual or sudden onset of symptoms, pain intensity minimal and maximal (VAS: 0-100 mm), degree of fatigue minimal and maximal (VAS: 0-100 mm), and less work due to complaints, unemployment, fully working, other reasons.

The following physical examination tests were performed: long dorsal sacroiliac ligament, mobility by video registration, active straight leg raising (ASLR) test, performance of activities of daily living without an increase in pain, posterior pelvic pain provocation (PPPP) test, and isometric force of hip abduction and adduction.[7] The long dorsal sacroiliac ligament test (0= no pain; 1= complaint of pain without grimace, flinch, or withdrawal [mild]; 2 = pain plus grimace or flinch [moderate]; 3= the examiner is not able to complete the test because of withdrawal [unbearable] score is positive when bilateral sum score is ≥ 2 (score range=0-6; higher score indicates severity of the pain provocation test). Mobility by video registration assessed range of motion of the pelvis in flexion, the low back in
flexion, and the pelvis + low back in flexion. The ASLR test was scored by the GP and the patient (0= not difficult at all, 1= minimally difficult, 2= somewhat difficult, 3= fairly difficult, 4= very difficult, 5= unable to do) is positive when the bilateral sum score is ≥ 2 (score range= 0–10; higher score indicates the severity of the load transfer disturbance from LBP). Activities of daily living (e.g., walking or bicycling in minutes [0 –15, 16–30, 31–60, ≥ 61]) without an increase in pain were assessed. The PPPP test, unilateral or bilateral (0= no pain, 1= pain unilaterally, 2= pain bilaterally) is positive when the bilateral sum score is ≥ 2 (0–2). Finally, isometric force of hip abduction (score: best to worse > 196–0 N) and adduction (score: best to worse > 129–0 N) were measured.[7]

Statistical analyses

Course of disability. Descriptive analyses were used to describe the patients' scores on disability at baseline and at 2-, 5-, and 12-months follow-ups. Also described were the 2 definitions of recovery: 30% improvement in QBPDS score compared to baseline and the absolute recovery (≤ 20 points on the QBPDS at follow-up measurement). These analyses were done on the entire data set, including missing values.

Model building. All of the measures used in this study were conducted during normal daily practice of the rehabilitation center. Relevant factors were categorized or dichotomized for enhance more easy clinical interpretation of the results.

Model building was done using the following steps:
Step 1. Eligible prognostic factors were identified which were highly correlated (r > 0.8). This was the case for the B200 Isostation (strength in flexion, extension, lateroflexion, rotation) and the SCL-90 (items 1-8). Only the B200 extension and the total score item 9 of the SCL-90 were included in the analysis.[21]
Step 2. Continuous factors were checked for linearity using spline regression curves. This step revealed a nonlinear relationship between BMI and the QBPDS score for disability. Therefore, BMI was changed to a categorical variable, which eases clinical interpretation.[21]
Step 3. Imputation of missing values in the data was carried out by multiple imputations. As a primary analysis, a total of 5 imputed datasets were used.[21-23] As a sensitivity analysis, the results were compared when 40 datasets were imputed. This number was selected because in the initial analysis, before backward selection (as a next step), about 40% of some of the patient data was missing. We also compared the results with complete-case analysis (CCA) (i.e., all patients with missing data were excluded from the analyses).[21-23]
Step 4. The most important prognostic variables were selected using a multivariable logistic regression analysis (stepwise method, backward: likelihood ratio $P < 0.157$).[24-27] The selection of variables was performed over all the imputed datasets using Rubin's rules of multiple imputation.[28] To assess whether the level of significance influenced the selection of predictors in the final prognostic model for all methods described in step 3, the selection of variables was repeated with *P* values of 0.05 and 0.157. A sensitivity analysis also was performed using QBPDS cut-off values of ≤ 10 and ≤ 39 points.[1]

Model performance

We checked the performance of the model with regard to the goodness of fit (Hosmer-Lemeshow test), the explained variation, and the discriminative ability. The explained variation of the model is estimated by Nagelkerke's R^2 statistic. Explained variation is the extent to which the outcome can be predicted by the model in the current datasets. The discriminative ability is reflected by the area under the receiver operating characteristics curve (AUC). The AUC represents the ability of the prognostic model to discriminate between patients who will recover from disability and those who will not recover from disability and ranges from 0.5 (chance) to 1.0 (perfect discrimination).[29]

Bootstrapping techniques were used to internally validate our models (ie. to simulate the performance with respect to the explained variance and the AUC in comparable patient datasets).[25,26,30,31] All analyses were done using SPSS version 18.0 (SPSS Inc, Chicago,Illinios) and R software (R Foundation for Statistical Computing, Vienna, Austria).

Role of the funding source

This study was financially supported by the Rotterdam University of Applied Sciences and the Department of General Practice, Erasmus MC, Rotterdam, the Netherlands.

Results

This study included 1,760 patients with CNLBP (mean age= 40.1 years, SD 10.6; 74.3% women) (Figure 1). Of these patients, 1,696 (96.4%) completed the 2-month multidisciplinary treatment, 1,564 (88.9%) participated in the 5-months follow-up, and 965 (54.8%) completed the 12-months follow-up. Table 1 presents the baseline characteristics of the 1,760 patients and the distribution of the candidate prognostic factors.

Table 1. *Baseline characteristics of study participants with chronic non-specific low back pain (CNLBP)*[a]

Characteristic	Patients (n=1,760)	Missing value n (%)
No. of female patients	1,307(74.3)	0
Age (y), M (SD)	40.1(10.6)	0
Demographic factors		
Low education	716(40.7)	71(4.0)
Marital status, living with one adult	1,515(86.1)	46(2.6)
Clinical status		
BMI > 25 kg/m^2	783(44.5)	88(5.0)
Duration of complaints (y), M (SD)	7.7(8.8)	0
Cause reported by patient:		23(1.3)
1 Accident/wrong movement	374(21.3)	
2 After physical overload	73(4.1)	
3 During pregnancy or after delivery	586(33.3)	
4 Pelvis/back surgery or after HNP	32(1.8)	
5 Unknown	672(38.2	
Previous revalidation program	186(10.6)	101(5.7)
Comorbidity	275(15.6)	88(5.0)
LBP intensity (VAS in mm), M (SD)		
present pain intensity	55.5(23.0)	5(0.3)
Course of pain intensity due to CNLBP in the previous 3 mo		52(3.0)
1 Stable pain intensity	865(49.1)	
2 Increased pain intensity	723(41.1)	
3 Decreased pain intensity	120(6.8)	
Degree of fatigue LBP (VAS in mm), M (SD)		
Present fatigue	56.5(26.6)	118(6.7)
Disability (QBPDS), M (SD)	51.7(15.6)	8(0.5)
Psychological factors		
Fear avoidance (TSK), M (SD)	36.7(7.3)	50(2.8)
SCL-90 (item 9), M (SD)	149.3(39.7)	227(12.9)
SF-36 (health-related quality of life)		
PCS	31.8(7.1)	493(28.0)
MCS	46.5(10.3)	493(28.0)

Characteristic	Patients (n=1,760)	Missing value n (%)
Work-related factors		
Employment status benefit	924(52.5)	353(20.1)
Work participation		161(9.1)
1 100% working	391(22.2)	
2 0-99% working	1,059(60.2)	
3 not working b	149(8.5)	
Physical examination		
ADL function, duration > 31 min without pain increase		
1 Walking	410(23.3)	10(0.6)
2 Sitting	432(24.5)	13(0.7)
3 Standing	106(6.1)	9(0.5)
B200 Isostation (strength) (N), M (SD)		
1 Extension	81.6(45.8)	107(6.1)

a Values are numbers (percentages) unless stated otherwise, of the entire data set of 1,760 patients. BMI = body mass index, HNP= herniated nucleus pulposus, LBP = low back pain, VAS = visual analogue scale, QBPDS = Quebec Back Pain Disability Scale, TSK = Tampa Scale for Kinesiophobia, SCL-90 = Symptom Checklist-90; SF-36 = Medical Outcomes Study36-Item Short Form Health Survey, PCS = Physical Component Summary, MCS = Mental Component Summary, ADL= activities of daily living. Missing values ranged from 0.5% (n=9) to 28% (n=493).

b Not working= currently not working because of in search of new work or seeking due to family care responsibilities or being retired.

Course of disability

At 2-months follow-up (n=1,696) the disability scores on the QBPDS decreased to a mean of 31.7(SD= 15.2) versus. a mean of 51.7 (SD= 15.6) at baseline. At 5- and 12-month follow-ups, these scores decreased to a mean of 31.1 (SD= 18.2) and 29.1 (SD= 20.0), respectively (Table 2).

The predefined outcomes regarding recovery on the QBPDS disability score at follow-up showed the following results: (1) compared with baseline, 1,058 patients (62.6%) reported a 30% improvement in disability after 2 months therapy, 955 patients (61.3%) reported improvement at the 5-months follow-up, and 611 patients (63.4%) reported improvement at the 12-months follow-up; and 2) for absolute recovery, 46 patients (2.6%) had a score ≤ 20 on the QBPDS at baseline; however, this finding is explained by the fact that additional patients were included for therapy based on other outcomes, such as pain intensity, quality of life or work participation.[7] After 2 months therapy, 409 patients (24.1%) scored ≤ 20 on the QBPDS; at 5- and 12 month follow-ups these numbers were 484 (30.9%) and 370 patients (38.3%), respectively.

Table 2. *Course of disability scores in patients with chronic non-specific low back pain at 2, 5 and 12-months follow-up*[a]

Measure	Baseline (n=1,752)	2 months (n=1,696)	5 months (n=1,564)	12 months (n=965)
Disability (QBPDS): mean (SD)	51.7 (SD 15.6)	31.7 (SD 15.2)	31.1 (SD 18.2)	29.1 (SD 20.0)
30% improvement in disability (QBPDS), %		62.6%	61.3%	63.4%
Absolute recovery on disability score (≤ 20 points on QBPDS), %	2.6%	24.1%	30.9%	38.3%
Back Pain (VAS) mean (SD)	55.5 (23.0)	37.0 (23.8)	35.3 (26.1)	32.3 (26.9)
Quality of life (SF-36)				
PCS, mean (SD)	31.9 (7.1)	40.7 (8.2)	42.1 (10.1)	
MCS, mean (SD)	46.6 (10.3)	49.2 (9.4)	50.4 (9.8)	
Work participation,[b] mean (SD)	38.3 (43.1)		73.4 (44.9)	81.7(52.9)

[a] *QBPDS = Quebec Back Pain Disability Scale (range= 0-100, higher score means more disability), VAS = visual analogue scale (0-100, 0=no pain), SF-36 = Medical Outcomes Study 36-Item Short- Form Health Survey (range=0-100, higher score means better quality of life), PCS = Physical Component Summary, MCS = Mental Component Summary. Missing values ranged from 0.5% to 35.2%. SD= standaarddeviation*

[b] *work participation (0%-100%) included those patients with paid work (n= 1,608)*

30% improvement between baseline and 5- and 12-month follow-ups

Table 3 shows the results of the multivariable logistic regression analyses of the potential prognostic factors regarding recovery defined as a 30% improvement in disability measured on the QBPDS at 5- and 12-month follow-ups.

At 5-months follow-up, the prognostic factors were: being married or living with one adult, shorter duration of back complaints at baseline, younger age, higher disability score at baseline, no previous rehabilitation, decreased course of pain in the 3 months prior to baseline, more work participation at baseline, and higher scores on the SF-36 PCS and MCS. The AUC of this model was 0.68 and the explained variance was 12.8%.

At 12-months follow-up the prognostic factors were: being married or living with one adult, having no comorbidity, younger age, a higher education level, higher disability score at baseline, no previous rehabilitation, reporting low pain intensity at baseline, and a higher score on the SF-36 PCS. The AUC of this model was 0.66, and the explained variance was 10.7%.

With regard to internal validation of the model, the explained variance at 5-month follow-up was 12.8% and the AUC was 0.68 (before and after analyzing the internal validation); at 12-month follow-up these data were 10.7% and 0.66, respectively.

Table 3. *Multivariable models of prognostic factors for 30% improvement in chronic non-specific low back pain (CNLBP) disability at 5- and 12-month follow-up's*[a]

Variable	5-months follow-up			12-months follow-up		
	OR	95% CI	P	OR	95% CI	P
Married/living with one adult (yes/no)	1.32	0.93-1.87	.12	1.54	0.88-2.68	.12
Age	0.97	0.96-0.98	< .001	0.98	0.97-0.99	≤ .01
Disability at baseline (QBPDS)	1.04	1.03-1.04	< .001	1.03	1.01-1.04	≤ .001
Previous revalidation program (yes/no)	0.52	0.37-0.74	< .001	0.72	0.48-1.08	.11
Work participation	1.42	1.02-1.96	.04			
SF-36 PCS	1.08	1.06-1.11	< .001	1.06	1.04-1.09	< .001
SF-36 MCS	1.03	1.02-1.04	< .001	1.02	1.00-1.03	.05
Course of pain intensity due to CNLBP in the previous 3 mo (1= increase of pain)	1.05	0.84-1.32	.65			
Course of pain intensity due to CNLBP in the previous 3 mo (2=decrease of pain)	1.66	1.05-2.62	.03			
Duration of complaints	0.98	0.97-0.99	.01			
Comorbidity				0.61	0.42-0.90	.02
Education level				1.45	1.01-2.07	.04
Pain intensity at baseline (VAS)				0.99	0.99-1.00	.09

[a] *95% CI= 95% confidence interval, OR = odd ratio(an OR > 1 reflects a higher probability of 30% recovery for the outcome back pain disability and an OR < 1 reflects a lower probability of 30% recovery for the outcome back pain disability, compared with the reference category; OR estimated after multiple imputation [n=5 datasets] with P value of.157, VAS = visual analogue scale, QBPDS = Quebec Back Pain Disability Scale, SF-36 = 36-Item Short-Form Health Survey, PCS = Physical Component Summary, MCS = Mental Component Summary. The variable "course of pain intensity due to CNLBP in the previous 3 mo" is a category value of 3 (0=stable, 1= increase of pain, 2=decrease of pain).*

Sensitivity analysis. Repeating the analysis with P values of 0.05 or 0.157, and using a CCA or 5 or 40 imputed datasets, resulted in more or less similar prognostic factors for a 30% improvement in recovery at 5- and 12-month follow-ups (Table 3). At 5-months follow-up, only the factor being married or living with one adult was excluded in all final models. At 12-months follow-up, the SF-36 MCS and previous rehabilitation were included only once. The various models included 5 to 10 factors with an AUC range of 0.64 to 0.68 (exact data can be provided by the first author).

Absolute recovery (QBPDS score ≤ 20 Points) at 5- and 12-month follow-ups

Table 4 shows the results of the multivariable logistic regression analyses of the potential prognostic factors for absolute recovery (QBPDS score ≤ 20) at 5- and 12-month follow-ups. The final prognostic model at 5-month follow-up included shorter duration of complaints at baseline, younger age, lower disability score at baseline, no psychoneurosis (SCL-90 item 9) and higher scores on the SF-36 PCS and MCS. The AUC of this model was 0.58 and the explained variance was 2.7%.

At 12-month follow-up, absolute recovery was associated with a greater baseline strength in the trunk (B200 Isostation), no comorbidity, ≤ 60 minute walking duration at baseline, shorter duration of complaints at baseline, younger age, lower disability score at baseline, lower pain intensity at baseline, and higher scores on the SF-36 PCS and MCS. The AUC of this model was 0.66 and the explained variance was 10.7%.

With regard to internal validation of the model, the explained variance at 5-month follow-up was 2.7% and the AUC was 0.58; for the 12-month follow-up these data were 18.6% and 0.72, respectively.

Table 4. *Multivariable models of prognostic factors for absolute recovery on chronic non-specific low back pain disability (CNLBP) (QBPDS ≤ 20 Points) at 5- and 12-month follow-up's*[a]

Variable	5-months follow-up			12-months follow-up		
	OR	95% CI	P	OR	95% CI	P
Duration of complaints	0.98	0.97-1.00	.05	0.98	0.97-1.00	.05
Age	0.98	0.96-0.99	< .001	0.98	0.97-0.99	< .01
Disability at baseline (QBPDS)	0.97	0.96-0.98	< .001	0.99	0.98-1.00	.09
SF-36 PCS	1.07	1.04-1.10	< .001	1.05	0.99-1.11	.05
SF-36 MCS	1.03	1.01-1.05	.01	1.03	1.00-1.06	.05
SCL-90 (item 9)	0.99	0.99-1.00	.08			
B200 Isostation extension				1.00	1.00-1.01	.09
Comorbidity				0.62	0.37-1.03	.07
Duration of walking 1 (0-15 min)				1.13	0.85-1.49	.40
Duration of walking 2 (16-30 min)				1.46	0.86-2.49	.15
Duration of walking 3 (31-60 min)				1.63	1.00-2.66	.05
Pain intensity at baseline (VAS)				0.99	0.98-1.00	.08

[a] *95% CI= 95% confidence interval, OR = odd ratio(an OR > 1 reflects a higher probability of < 20 point Quebec Back Pain Disability Scale [QBPDS] for the outcome back pain intensity and an OR < 1 reflects a lower probability of < 20 point QBPDS for the outcome back pain intensity, compared with the reference category; OR estimated after multiple imputation [n=5 datasets] with P value of .157), VAS = visual analogue scale, SCL-90 (item 9)= Symptom Checklist-90, SF-36 = 36-Item Short-Form Health Survey. PCS = Physical Component Summary, MCS = Mental Component Summary. The variable 'duration of walking' is a category value of 4 (1=0-15 min, 2=16-30 min, 3= 31-60, 4= > 61 min).*

Sensitivity analysis. Repeating the analysis with *P* values of 0.05 or 0.157, and using a CCA or 5 or 40 imputed datasets, resulted in more or less similar results for the prognostic factors as reported in the 5-month follow-up model (Table 4). At the 12 month, comorbidity, lower pain intensity (VAS), and the SF-36 MCS were included in all final models (except for 1 or 2 of the models). The other factors mentioned above for a QBPDS score ≤ 20 were reported or excluded only once or twice. The various models had 4 to 11 factors with an AUC range of 0.70 to 0.76.

Performing the sensitivity analysis with QBPDS cut-off scores of ≤ 10 and ≤ 39 points, yielded similar results. Only at the cut-off score ≤ 39 points did some new prognostic factors emerge (i.e., higher education and previous rehabilitation at the 5-month follow-up, no psychoneurosis (SCL-90 item 9) at 12-months follow-up, and more work participation at baseline). At 12-month follow-up the SF-36 MCS was excluded at the QBPDS score ≤ 39 points. The various models had 5 to 9 factors, with an AUC range of 0.68 to 0.82 (exact data can be provided by the first author).

Discussion

Main study findings

After 2 months of multidisciplinary therapy, patients with CNLBP showed a decrease in mean reported disability. At 5- and 12-month follow-ups, this trend continues but with a slight decrease in 30% improvement and also in absolute recovery (QBPDS score ≤ 20).

The present study explored potential prognostic factors at 5- and 12-month follow-ups for the outcome 30% improvement in recovery from baseline and absolute recovery (QBPDS score ≤ 20 score). All patients received multidisciplinary therapy based on behavioral principles.[7]

For 30% improvement in recovery compared with baseline, the prognostic factors at both 5- and 12-month follow-ups ($P < .157$) were married or living with one adult, younger age, higher disability at baseline, no previous rehabilitation, and a higher baseline score on the SF-36 PCS and MCS.

Younger age, less disability at baseline, shorter duration of back complaints at baseline, and a higher baseline score on the SF-36 PCS and MCS were predictors of absolute recovery (QBPDS score ≤ 20 points) at both 5- and 12-month follow-ups. Despite having either severe or less severe disability at baseline, the difference between the 30% improvement (odds ratio > 1) and absolute recovery (odds ratio < 1) was relatively small (ie, an odds ratio (95% confidence interval) of around 1.0. We can expect that patients with severe disability (high scoring on the QBPDS) at baseline will change 30% over time easier than going from a high score to ≤ 20 points. For example, a patient with a baseline score of 80 points on the QBPDS will easier decrease 30% (around 24 points) in his disability scale at follow up, then go from 80 points to less than 20 points. Thus, the choice of outcome definition makes the difference.

The sensitivity analysis shows similar prognostic factors for the defined recovery at both 5- and 12-month follow-ups; this finding indicates that the outcome recovery defined with QBPDS disability scores and the identified prognostic factors are similar, irrespective of the duration of follow-up within 1 year. At the 5-month follow-up, a shorter duration of back complaints at baseline was a positive prognostic factor for both 30% improvement and absolute recovery.

At the 12-month follow-up, having no comorbidity and less pain at baseline were positive prognostic factors for both outcomes. In general, younger patients and those with higher scores on the SF-36 PCS and MCS, had a higher odds ratio to recover from CNLBP.

Strengths and Limitations

Prognostic model research includes 3 main phases: model development (including internal validation), external validation, and investigations of impact in clinical practice.[32] To improve the quality of a prognostic study, the following considerations are important: (1) dealing with missing data, (2) modelling continuous prognostic factors, (3) the complexity of the model, and (4) checking the model assumptions.[32] Our study aimed to develop several models and determined the internal validation of these models. To our knowledge, this is one of the first studies that examined prognostic factors for good recovery of patients with CNLBP treated multidisciplinary team.

In the present study, one of the limitations is that several factors had missing values (range= 0.5%-28%). We decided to impute the missing data using information on the other variables in the dataset.[33] At the 5- and 12-month follow-ups, 11.1% and 45.2% of the patients, respectively, failed to return the follow-up questionnaires for a variety of reasons (e.g., vacation, envelope not stamped, recovered from disability, did not find it necessary, starting another intervention). The multiple imputation procedure is assumed to be more valid than simply omitting these participants from the analysis. Also, not including the full study sample but only those patients with complete data reduces the sample size and power and thus, the model's validity.[24,30,33] In addition, performing sensitivity analyses that compare the data with more imputed datasets (n=40 and n=5), with *P* value levels of .05 and .157, and the CCA improves the validation of the model.[21,23,29,30] The sensitivity analysis revealed little or no difference in the identified prognostic factors. This findings indicates that the selection of the most important predictors was not strongly influenced by the selection criterion or by the amount of missing data. In all analyses, the CCA showed slightly higher standard errors (SEs) and coefficients compared to the imputed datasets. This finding indicates that, as expected, both the power and precision were increased by imputation.[34]

We dichotomized the outcome disability as recommended in some studies of LBP[11,35,36] for ease of interpretation by clinicians and patients. Dichotomising continuous variables such as the QBPDS has some implications for the results: (1) information loss on patients outcome, (2) patients close to but on opposite sides of for example the cut-off point of 30% improvement are characterised as being very different rather than very similar, and (3) using 2 groups (e.g., improved versus. not improved) conceals any nonlinearity in the relation between the variable and outcome.[37]

Furthermore the values odds ratio (95% confidence interval), variance and AUC demonstrated in this study remained quite similar. An AUC of 0.5 to 0.7 is considered moderate discrimination; the explained variance ranged between 2.7% and 12.8% which indicates that other potential prognostic factors (e.g., physical parameters) should be considered to predict recovery of a patient. However, other studies in the field showed similar low ranges of explained variance.[9]

This current survival cohort represent patients with CNLBP persisting over a long time (mean= 7.7 years). Thus, the clinical course could differ between the patients recruited in an inception cohort, those with more complex in condition, and those having more complex factors that influence recovery.[38] However, this study represented patients who did not recover in the Dutch primary care system and were eligible for a rehabilitation treatment. Therefore, comparison of the baseline characteristics may differ from other cohorts on CNLBP because most of them are inception cohorts and recruited in primary care setting.[5] The generalizability of the results is limited because the patients were recruited in a rehabilitation centre for tertiary care and received multidisciplinary therapy. However, this is a group of patients who some patients as well as clinicians would believe cannot recover, whereas the present study shows potential for the future.

Comparison with the literature

In the present study, more patients were improved during 12-months follow-up based on a cut-off of 30% improvement compared with baseline than on a score of ≤ 20 points on the QBPDS. However, patients with a lower baseline score have less potential for improvement, and patients with more severe baseline disability need to perceive a greater improvement in order to feel that it is relevant.[39] This findings promote discussion as to which cut-off point to use in daily practice: the clinical change (30%) that can be measured to show that someone is improving or to consider the wish of the patient who wants an absolute recovery. One possibility is to discuss these options in relation to the wishes and objections of the patient and clinician over time and perhaps combine these outcomes.

Our results do not support the findings of our previous systematic review,[9] except that fear of movement is not associated with disability at 5- and 12-month follow-ups. Perhaps, as reported by others authors,[4,40,41] the impact of fear of movement only plays a role in the transition from subacute to CNLBP. Nevertheless, because several multidisciplinary programs for patients with CNLBP mainly focus on fear of movement, the question arises whether this is an optimal choice for patients in this phase. Furthermore, we found several prognostic factors that have a positive association with disability such as younger age, and less pain intensity and more work participation at baseline; our systematic review found no studies with these associations with disability.[9] In another study (149 patients with acute or CNLBP for 1 month, treated with manual therapy and spine strengthening exercises until discharge) the outcome disability was measured with Oswestry Disability Index at

a mean follow-up of 35.7 days (SD= 29.9); the reported prognostic factors similar to those in the present study were shorter duration of symptoms, lower Oswestry Disability Index score at baseline, and younger age.[42] In essence, prognostic factors based on a single outcome measure may not fully represent all aspects of recovery from a multidimensional condition such as CNLBP.[42] Our previous review also indicates that disability is not an ''isolated'' condition but is associated with, for example, the degree of pain.[9]

Outcome Measurement

This study benefited from the large sample size, its prospective design, and patients' self-report. In the study of Davidson and Keating,[43] the Oswestry Disability Questionnaire, the SF-36 Physical Functioning scale, and the QBPDS had sufficient reliability and scale width to be applied in an ambulatory clinical population with low back problems. The responsiveness of the questionnaires was similar, and the authors concluded that one questionnaire cannot be preferred over another based on the magnitude of the absolute values of responsiveness indexes.[43]

The present study shows that, when determining the cut-off point for a clinically relevant recovery from disability, there is little difference between the two definitions used (i.e., 30% improvement and absolute recovery defined as a QBPDS score ≤ 20) with regard to the identified prognostic factors. However, Table 2 shows that fewer patients were recovered at 12-month follow-up based on the absolute recovery compared with 30% improvement option (i.e., 38.3% versus 63.4%, respectively). Undoubtedly the cut-off points will differ based on the severity of symptoms within the study population, the condition of interest, and other factors.[42] A study in which the global perceived effect scale of the patient (e.g., ''completely recovered'') is compared with the score on the QBPDS may provide more insight into the most relevant cut-off point.

Clinical Value

This study shows that in patients with CNLBP, positive predictors for recovery at 5- and 12-month follow-ups are: younger age, higher scores on the SF-36 PCS and MCS and scoring higher on disability at baseline. For the 5-month follow-up, these positive predictors are shorter duration of complaints, and at 12-month follow-up, they are having no comorbidity and less pain at baseline. For daily practice, this study provides preliminary evidence for clinicians to estimate the prognosis for disability over a 1-year period based on easy-to-obtain baseline data. We have developed and internally validated prognostic model for recovery at 5- and 12-month follow-ups for patients with CNLBP in tertiary care. However, because the explained variance ranged from 2.7% to 12.8%, the results must be interpreted with caution.

Future Research

Future studies should identify the potential prognostic factors in different settings and over a longer period of time. These factors may provide more insight into the validity of the presented models. A subsequent step is external validation of the prognostic models with the aim to use them in daily practice.[25] Overall, the results of this study indicate that biopsychosocial factors may be important in the course of and changes in disability level at 5- and 12-month follow-ups and that some preliminary prognostic factors can be identified.

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All authors declare that there are no conflicts of interest.

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CHAPTER 6

Prognosis and course of work participation in patients with chronic non-specific low back pain: a 12-months follow-up cohort study

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Submitted

Abstract

Question. What is the course of work participation in patients with chronic non-specific low back pain (CNLBP) who followed a multidisciplinary treatment? Which prognostic factors are related to the course of work participation at 5 and 12-months follow-up?
Design. A prospective cohort study.
Participants. A total of 1,608 patients (mean age 39.5 years) were included after diagnostic consultation in a multidisciplinary rehabilitation centre.
Intervention. A 2-month multidisciplinary rehabilitation program.
Outcome measures. Included were 23 potential prognostic factors of demographic, physical, clinical, psychological and work-related context. The outcome of interest was work participation.

Results. Patients reported an increase in work participation from (on average) 38% at baseline to 82% after 12 months. Baseline factors affecting outcome at 5-months follow-up were low back pain intensity, low work participation, duration of standing and the cause. The baseline factors younger age, higher education, lower work participation and higher mental scale component (SF-36) were associated with a 30% improvement in work participation at 12-months follow-up. Prognostic factors for absolute work participation (≥ 90% work-participation) at 5 months were being married, female, a high score on the disability (QBPDS) and physical component scale (SF-36), previous rehabilitation, not receiving sickness benefits, and higher work participation at baseline. Higher work participation at baseline and female gender were also prognostic factors at 12-months follow-up.
Conclusion. At 12-months follow-up, these patients had increased their work participation. Several baseline characteristics associated with improvement in work participation at 5- and 12-months follow-up were identified.

Introduction

Currently, much research on low back pain (LBP) focuses on progression from the acute to a chronic stage and prognosis within the chronic stages.[1,2] The natural course of LBP affects the ability to function in both work and personal life[3,4] and less than two-thirds of patients who develop chronic non-specific low back pain (CNLBP) recover within 12 months.[3]

An Australian study that defined complete recovery as patients that are 'recovered from pain, disability and work status, showed that the prognosis is less favourable for those who have taken previous sick leave for LBP, have more disability or severe pain intensity at onset of CNLBP (> 3 months), have a lower education level, and perceive themselves as having a high risk of persistent pain.[5]

Our systematic review[6] on prognostic factors of CNLBP at 12-month follow-up showed no association with the factor strength, and conflicting evidence for the association between return to work and age, sex, mobility and activities of daily living. At baseline, there was limited evidence for a positive influence of lower pain intensity and lower physical job demands on the outcome return to work.

More extensive information on the course and modifiable prognostic factors for improvement in work participation could be helpful for professionals to better inform their patients and to influence their return to work. Therefore, we formulated the following research questions:

1) What is the course of work participation of patients with CNLBP managed in a multidisciplinary rehabilitation centre after 5- and 12-months?
2) Which potential prognostic factors are associated with work participation in CNLBP patients at 5 and 12 months following a multidisciplinary treatment?

Method

Design

A prospective cohort study in CNLBP patients selected from a multidisciplinary outpatient rehabilitation clinic the Spine & Joint Centre (SJC) in Rotterdam, the Netherlands. All patients received several (postal) questionnaires and underwent a physical examination. Data were collected at baseline and at 2-, 5- and 12-months-follow-up.

The Medical Ethics Committee of the SJC approved the study protocol and all patients provided informed consent. Details on the study design are described elsewhere.[7]

Participants

All CNLBP patients were recruited between January 2003 and December 2008 at the SJC. Inclusion criteria were complaints lasting ≥ 3 months, aged ≥ 18 years, and previous unsuccessful treatment (e.g., physiotherapy) in primary or secondary care. For the analysis, in the present study, having a work contract at baseline was added as an extra inclusion criterion. Exclusion criteria were insufficient knowledge of the Dutch language, signs indicating radiculopathy, asymmetric Achilles tendon reflex and/or straight leg raise test restricted by pain in the lower leg, positive MRI findings for disc herniation, neoplasm, recent (< 6 months) fracture or surgery (< 6 months) of the lumbar spine, the pelvic girdle, the hip joint, or the femur, systemic disease of the locomotor system, and being pregnant or ≤ 6 months post-partum at consultation.

Intervention

The multidisciplinary treatment at the SJC centre used a bio-psychosocial approach consisting of 16 sessions of 3 h each during a 2-month period (total of 48 h). Patients were coached by a multidisciplinary team (e.g., a physical therapist, physician, health scientist, psychologist).[7]

Prognostic factors and outcome

The selection of relevant prognostic factors was performed in two steps; 1) the literature on prognosis for CNLBP and work participation was reviewed, and 2) a clinical group of experts on CNLBP composed a list of 47 prognostic factors. Using the Policy Delphi method, this list was scored for importance (scored on a 4-point Likert scale ranging from 1=very important to 4=not important) by 8 experts working in different clinical settings.[8,9] A total of 23 prognostic factors were finally included, complying with the rule of at least 10 events per variable in the analysis[10] (see Box 1).

Box 1. *The 23 potential prognostic factors*

Continuous variables

1 Age
2 Duration of back pain in years
3 Present pain intensity (VAS: 0-100 mm)
4 Degree of present fatigue (VAS: 0-100 mm)
5 Quebec Back Pain Disability scale (QBPDS: 0-100)
6 Tampa scale for kinesiophobia (TSK, 17-68)
7 Short-form health survey 36 (SF-36);
Physical Component Scale (PCS) (range 0 ''low quality of life''-100 points)
8 Short-form health survey 36 (SF-36;
Mental Component Scale (MCS) (range 0 ''low quality of life''-100 points)
9 Symptom Checklist 90 (SCL90;item 9; psychoneuroticism)
10 Work participation (0-100%)
11 B200 Isostation (strength back extension in Newton)

Categorical variables

12 Body Mass Index (BMI ≤ 24.9/ 25-29.9/ ≥ 30 kg/m^2)
13 Cause of back pain (accident movement; after physical load; during pregnancy or after delivery; unknown; surgery pelvis/back or HNP)
14 Course of pain in the previous 3 months (stable; increased; decreased)
15 Duration of walking (0-15/ 16-30/ 31-60/ > 61 minutes)
16 Duration of sitting (0-15/ 16-30/ 31-60/ > 61 minutes)
17 Duration of standing (0-15/ 16-30/ 31-60/ > 61 minutes)

Dichotomized variables

18 Gender
19 Comorbidity (no versus having one or more co-morbidities)
20 Marital status (being alone versus being married/living with one adult)
21 Level of education (< high school versus ≥ high school/university)
22 Previous rehabilitation treatment (no versus one or more previous rehabilitation treatments)
23 Sickness benefit (no versus all kinds of benefits from the government or employer)

The outcome was work participation, which was defined by dividing 'current work hours' by 'former work employment hours' prior to CNLBP.[7] Recovery of work participation was operationalised according to two definitions: 1) 30% improvement in work participation from baseline[11-13] and 2) absolute work participation, defined as ≥ 90% work participation at follow-up.[12,14,15]

Data analysis

Descriptive analysis was performed to describe the course of work participation and patient characteristics.

First, eligible prognostic factors were identified which were highly correlated ($r > 0.8$). This was the case for the B200 Isostation (strength in flexion, extension, lateroflexion, rotation) and the Symptom Checklist 90 (SCL90, items 1-8). Only the B200 extension and the total score (i.e., item 9) of the SCL90 were included in the analysis.[16] The con- tinuous factors were checked for linearity using spline regression curves which revealed a non-linear relationship between body mass index (BMI) and work participation.

For all five outcomes belonging to the same study design, the same 23 prognostic factors were included.[7] BMI was changed into a categorical variable. With regard to missing values, we applied multiple imputation of 5 datasets. Because in some patients 28% of data were missing, the results were compared with 40 datasets and complete case analyses (CCA).[16,17]

To develop our prognostic model, multivariable backward logistic regression analysis was performed and initially included 23 potential factors. The variables with the highest p-value were removed one by one, until all remaining variables had a p-value of < 0.157.[18-21] The selection of variables was done over all imputed datasets using Rubin's rules.[22] To assess whether the level of significance influenced the final prognostic model, the selection of variables was repeated with a p-value of 0.05. A sensitivity analyses was performed with different work participation cut-off values of 80% working and 100% working, and p-values of 0.05 and 0.157.[12]

The performance of the model was checked with regard to the goodness of fit (Hosmer-Lemeshow test), the explained variation, and the discriminative ability of the model. The explained variation of the model was estimated by Nagelkerke's R squared. Explained variation is the extent to which the outcome can be predicted by (the predictors in) the model in current dataset(s). The discriminative ability is reflected by the area under the receiver operating characteristic curve (AUC) [range 0.5 (chance) to 1.0 (perfect discrimination)].[23]

Bootstrapping techniques were used to internally validate the models, i.e. to simulate the performance with respect to the explained variance and the AUC in comparable patient datasets.[19,20,24,25]

Results

Study population

The original cohort consisted of 1,760 patients, of which 1,608 had a work contract at baseline and were included (Figure 1). Table 1 presents the baseline characteristics. Mean age of the patients was 39.5 (SD 9.8) years and 73.1% of the patients were female. Of all patients, 1,059 patients worked 0-99% of their 'former work employment hours' implying that they had either productivity loss, or partial or complete sick leave. At baseline, mean duration of back pain complaints was 7.3 (SD 8.2) years.

Of all participants, 1,557 (97%) completed the 2 months multidisciplinary treatment, 1,433 (89%) returned the 5-month follow-up and 886 (55%) returned the 12-month follow-up questionnaire. The main reasons for missing variables were incomplete or not returned questionnaires.

Course

Table 2 presents the course of work participation at baseline, and at 5 and 12-months follow-up. At baseline, mean work participation was 38.3% (SD 43.1), at 5 months this had increased to 73.4% (SD 44.9) and at 12-months follow-up to 81.8% (SD 52.9). Regarding the 30% work improvement, 30.3% reported work participation at 5 months, increasing to 60.5% at 12-months follow-up. Absolute work participation (≥ 90%) was present in 25.4% at baseline, 43.2% at 5 months and in 52.0% at 12-months follow-up.

Prognostic factors at 30% improvement work

Table 3 shows the multivariable backward stepwise logistic regression analysis between baseline variables and work participation at 5- and 12-months follow-up. At 5 months the following prognostic factors were present: low back pain intensity, low work participation, duration of standing (31-60 min) and the cause (accident or wrong movement) at baseline, with an explained variance of 59% and an AUC of 0.89.

At 12-months follow-up the multivariate regression model (AUC=0.90) consists of 4 prognostic factors explaining 60% of the variation: younger age, higher education, low work participation at baseline, and a higher Mental Component Summary (MCS) on the SF-36 at baseline. With regard to internal validation of the model, the explained variance was 59% and 60%, respectively, with an AUC of 0.89 and 0.90 at 5 and 12-months follow-up, respectively.

The sensitivity analysis at 5 months showed that low back pain intensity and lower work participation were the most frequently mentioned factors. At 12-months follow-up, higher education level and lower work participation were most often reported. The factor lower work participation was present in all models at 5 and 12 months. The CCA also revealed other factors in both the 5 and 12-months follow-up. At 5-months follow-up the explained variance was 47% and the AUC was 0.83-0.92 compared with 10-60% and 0.60-0.91, respectively, at 12-months follow-up.

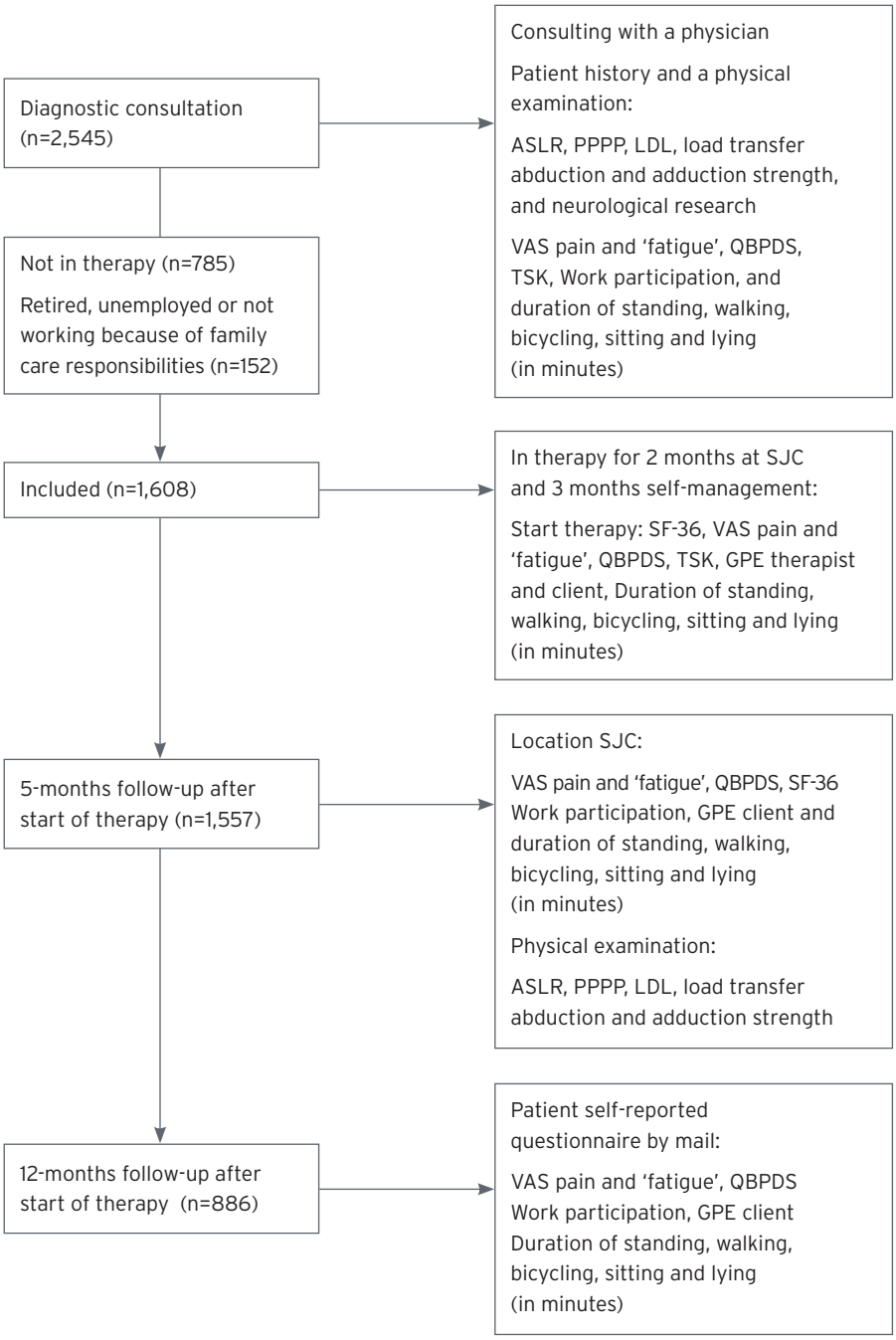

Figure 1. *Study design*

SJC=Spine & Joint Centre; ASLR= Active Straight Leg Raise test; PPPP= Posterior Pelvic Pain Provocation test; LDL= longum dorsal sacro-iliac ligament; VAS= Visual Analogue Scale; QBPDS= Quebec Back Pain Disability Scale; SF-36=Short Form; TSK= Tampa Scale Kinesiophobia; GPE=Global perceived effect.

Table 1. *Baseline characteristics of 1,608 patients with chronic non-specific low back pain (CNLBP)*[a]

Characteristic	Patients (n=1,608)	Missing values(%)
Number of female patients	1,176(73.1)	0
Age in years: M (SD)	39.5(9.8)	0
Demographic factors		
Low education level*	630(39.2)	3.7
Marital status/living with one adult*	1,386(88.2)	2.7
Clinical status		
Patients with BMI > 25*	495(30.8)	4.7
Duration of complaints in years: M (SD)	7.3(8.2)	0
Cause reported by patient:		0.81
1 accident/wrong movement	349(21.7)	
2 after physical overload	62(3.9)	
3 during pregnancy or after delivery	552(34.3)	
4 surgery pelvis/back or after HNP	27(1.7)	
5 unknown	605(37.6)	
Previous revalidation program*	169(10.5)	5.5
Comorbidity	234(14.6)	4.7
Pain intensity LBP (VAS in mm): M (SD)		
1 present pain intensity	55.4(22.9)	0.12
Pain intensity due to CNLBP in the previous 3 months		2.5
1 stable pain intensity	804(51.3)	
2 increased pain intensity	648(41.4)	
3 decreased pain intensity	115(7.3)	
Degree of fatigue LBP(VAS in mm):M(SD)*		
1 present fatigue	56.67(26.6)	6.2
Disability (QBPDS): M (SD)	51.69(15.4)	0.19
Psychological factors		
Fear avoidance (TSK): M (SD)	36.6 (7.3)	2.6
SCL90 item 9 M(SD)	149.3(40.0)	12.4
SF-36 (health-related quality of life)		
PCS	31.8(7.1)	27.4
MCS	46.5(10.3)	27.4
Work-related factors		
Sickness benefit	891(67.1)	17.4
Work participation		9.8
1 100% working	391(24.3)	
2 0-99% working	1,059(65.9)	
Physical examination		
ADL function – duration > 31 min without pain increase		
1 walking	367(22.8)	0.31
2 sitting	395(24.6)	0.56
3 standing	96(6)	0.37
B200 Isostation (strength) (Newton): M(SD)		
1 extension	82.6(46.3)	5.8

a these factors were reported when therapy started, or gathered from the personal status; values are numbers (percentages) unless stated otherwise; M = mean; SD = standard deviation; BMI = Body Mass Index; CNLBP = chronic non-specific low back pain; VAS = Visual analogue scale; QBPDS = Quebec Back Pain Disability Scale; TSK = Tampa Scale Kinesiophobia ; SCL-90 (item 9) = Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary; ADL= activities of daily living. Missing values ranged from 0.12% (n=2) to 27.4% (n=441). For work participation (n=1608 had a work contract) in 9.8% of cases there were missing values for 'current work hours' at baseline, therefore work participation could not be calculated.*

Table 2. *Course of disability scores in patients with chronic non-specific low back pain (CNLBP) at 5- and 12-months follow-up*

Variable	Baseline (n=1,608, 1,405)	5 months (n=820)	12 months (n=589)
Work participation (mean, SD)	38.3 (SD 43.1)	73.4 (SD 44.9)	81.7 (SD 52.9)
30% improvement on work participation		30.3%	60.5%
		(170/560)	(125/376)
Absolute work participation (≥ 90%)	25.4%	43.2%	52.0%

CNLBP= chronic non-specific low back pain; mean (SD= standard deviation), n=number of patients. Missing values ranged from 12.6% to 36.2%.

Table 3. *Multivariable models of prognostic factors for 30% improvement in chronic non-specific low back pain, work participation at 5- and 12-month follow-ups*

Variable	5-months follow-up			12-months follow-up		
	OR	95% CI	p-value	OR	95% CI	p-value
Back pain at baseline (VAS)	0.99	0.98-1.00	0.026			
Duration of standing						
16-30 min	0.86	0.38-1.95	0.680			
31-60 min	0.39	0.15-1.06	0.065*			
61 min and longer	1.14	0.39-3.37	0.809			
Cause						
After physical overload	1.69	0.51-5.62	0.37			
During pregnancy or after delivery	1.27	0.53-3.05	0.56			
Unknown	1.37	0.82-2.27	0.22			
Surgery pelvis/back or after HNP	2.27	0.14-36.42	0.51			
Work participation (0-100%)	0.017	0.00-1.05	0.052	0.0095	(0.0024-0.0380)	< 0.001
Age				0.97	(0.95-1.00)	0.068
Education				2.11	(0.90-4.92)	0.075
SF-36 MCS				1.03	(0.99-1.07)	0.152

95% CI= 95% confidence interval, OR = odds ratio, an OR > 1 reflects a higher probability of 30% recovery for the outcome work participation and an OR < 1 a lower probability of 30% recovery for the outcome work participation, compared to the reference category. OR estimated after multiple imputation (n=5 datasets) with p-value of 0.157.
HNP= Hernia Nucleus Pulposus; SF-36 = Short Form; MCS = Mental Component Summary.

Prognostic factors for absolute work participation (≥ 90% at work)

Table 4 shows the results of the patients working ≥ 90% of their contract hours at 5- months and 12-months follow-up. At 5-months the factors remaining in the final model yield an explained variance of 30% with an AUC of 0.78. These factors were: being married or living with one adult, being male, high score on disability at baseline, previous rehabilitation, no sickness benefit, high work participation at baseline, and a high Physical Component Scale (PCS) score on the SF-36 at baseline.

At 12-months follow-up the explained variance was 17%, with an AUC of 0.70. Higher work participation at baseline and being male were identified as prognostic factors.

At 5 and 12-months follow-up, internal validation of the model revealed an explained variance of 30% and 17%, respectively, with an AUC of 0.78 and 0.70, respectively.

At 5-months follow-up, sensitivity analyses demonstrated similarity in almost all of the prognostic factors between the different models. Only the CCA included some different factors. Work participation and being male were reported most frequently. For the 12-months analysis, higher work participation was present in every model, as were several other factors similar to the presented final models. At 5-months follow-up the explained variance was 28-30% with AUCs of 077-0.78 compared with 11-17% and AUCs of 0.66-0.70 at 12-months follow-up.

Table 4. *Multivariable models of prognostic factors for absolute recovery on chronic non-specific low back pain (CNLBP), work participation (90%) at 5- and 12-month follow-ups*

Variable	5-months follow-up			12-months follow-up		
	OR	95% CI	p-value	OR	95% CI	p-value
Married/living with one adult (no/yes)	1.72	(1.12-2.65)	0.01			
Disability at baseline (QBPDS)	1.00	(0.997-1.02)	0.15			
Previous revalidation program (no/yes)	1.85	(1.14-2.98)	0.01			
Sickness benefit (no/yes)	0.52	(0.24-1.10)	0.08			
Work participation (0-100%)	4.86	(2.35-10.04)	< 0.001	5.22	(3.47-7.85)	< 0.001
SF-36 PCS	1.05	(1.02-1.07)	< 0.001			
Gender (female/male)	1.99	(1.24-3.20)	0.09	1.79	(1.25-2.55)	0.003

95% CI= 95% confidence interval, OR = odds ratio, an OR > 1 reflects a higher probability of 90% recovery for the outcome work participation and an OR < 1 a lower probability of 90% work participation compared with the reference category. OR estimated after multiple imputation (n=5 datasets) with p-value of 0.157. QBPDS= Quebec Back Pain Disability Scale; SF-36= Short Form 36 questionnaire, PCS = Physical Component Summary.

Discussion

New and important findings of this current study are that the course of work participation showed a clear increase during the 12-months follow-up and various prognostic factors were identified of which some can be influenced by a clinician.
To our knowledge, only long-term follow-up (≥ 6 months) of prognostic factors have previously been reported.[6] Short-term follow-up (≤ 6 months) of work recovery is presented for the first time for this population with CNLBP.

In the 5-months analysis the 30% work improvement is associated with (at baseline) low back pain intensity, low work participation, duration of standing (31-60 min) and the cause of pain (accident or wrong movement), where as at 12-months analysis improvement is associated with (at baseline) younger age, higher education, higher MCS and lower work participation. In the 5-months analysis prognostic factors for absolute work participation were (at baseline) being married, male gender, high QBPDS score or PCS score, previous rehabilitation, no sickness benefits, and higher work participation. In the 12-months analysis (at baseline) higher work participation and being male were identified. No clear reason emerged for the difference between the definitions and models at 5 and 12-months follow-up, and the sensitivity analysis showed similar result.

A systematic review by Guzman et al. provides evidence that intensive multidisciplinary bio-psycho-social rehabilitation with a functional restoration approach improves pain and function in patients with CNLBP. Some trials reported improvements in work readiness, whereas others showed no significant reduction in sickness leave.[26] Our study population received a therapy aimed at physical/functional recovery, which may partly explain the positive course of work participation.

In our systematic review, baseline lower pain intensity and physical job demands were found to be positive prognostic factors at 12 months.[6] In the present study, baseline lower back pain intensity was associated with a < 30% improvement at 5-months follow-up; details on physical job demands were not included in the present study.

This study has some limitations. First, it is unknown whether the patients had the same contract work hours at baseline and one year later. Also, it is unknown if patients returned to work to their former job, or to a job with adjustments, or to another job; details on contractual working hours were asked only at follow-up. A second limitation is that we were unable to limit missing data (0-27.4%) at baseline and during the following year (45% loss of patients at 12 months), because data were collected during the daily process in rehabilitation care. However, we assume our missing data to be 'at random', which is not uncommon in long-term follow-up. Imputation of data is a valid method[16], and the sensitivity analyses showed similar results with a range of (low to high) explained variances (17-60%) and AUCs (0.66-0.90).

The present study is part of larger investigation on a number of outcome measures, besides that of work participation.[7] For all outcomes, the same 23 prognostic factors were used in the multivariate regression models. Therefore, certain other variables such as socio-economic variables (e.g. bread winner), occupational variables (e.g., social security agency), job characteristics (e.g., job satisfaction) and other factors such as work attitude and help with personal problems, were not selected in this study.[27] It is also possible that other potential factors have not been addressed in the present study.

Clinical, work and psychosocial-related variables contribute to the development of improvement from CNLBP. The most promising variables over the 12 months appear to be staying at work and low psychosocial factors at baseline. These variables are relevant for clinicians in order to advise their patients with respect to treatment strategy and optimal chance to improve over time.

We used contemporary statistical methods to internally validate the prognostic models. These methods reduce the tendency for variable selection procedures to produce overly optimistic estimates of model performance.[19] Further research is recommended in other settings to enable clinicians to eventually apply these models.[18]

Ethics: The study was approved by the Ethics Committee of the Spine & Joint Centre and Erasmus Medical Centre Rotterdam. Informed consent was provided by all eligible patients; their written consent was obtained before start of the diagnostic procedure and the present study.

Competing interests: All authors and organisations have nothing to declare.

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CHAPTER 7

Prognostic factors and course for successful clinical outcome quality of life and patients' perceived effect after an cognitive behaviour therapy for chronic non-specific low back pain: a 12-months prospective study

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Abstract

This study investigates the clinical course of and prognostic factors for quality of life and global perceived effect (GPE) in patients treated for chronic non-specific low back pain at 5 and 12-months follow-up. Data from a prospective cohort (n=1,760)

of a rehabilitation center were used, where patients followed a 2-months cognitive behavior treatment. Quality of life was measured with the Short Form 36-item Health Survey (SF-36). The outcome 'improvement in quality of life' was defined as a 10% increase in score on the SF-36 at follow-up compared with baseline. On the GPE scale, patients who indicated to be 'much improved' were coded as 'clinically improved'. Multivariable logistic regression analysis included 23 baseline characteristics. At 5-months follow-up, scores on the SF-36 Mental Component Scale (SF36; MCS) and the Physical Component Scale (SF-36; PCS) had increased from 46.6 (SD 10.3) to 50.4 (SD 9.8) and from 31.9 (SD 7.1) to 46.6 (SD 10.3), respectively. At 5-months follow-up, 53.0% of the patients reported clinical improvement (GPE), which increased to 60.3% at 12-months follow-up. The 10% improvement in quality of life (SF-36 MCS) at 5-months follow-up was associated with patient characteristics and psychological factors. At 5-months follow-up, the 10% improvement in quality of life (SF-36 PCS) and GPE was associated with patient characteristics, physical examination, work-related factors and psychological factors; for GPE, an association was also found with clinical status. At 12-months follow-up GPE was associated with patient characteristics, clinical status, physical examination and work-related factors. The next phase in this prognostic research is external validation of these results.

Keywords. chronic non-specific low back pain; course; prognosis; psychological factors

Introduction

Chronic non-specific low back pain (CNLBP) is one of the most prevalent health problems.[1] Although it is known that physical, psychosocial and personal factors play a role, the way they interact with each other remains unclear. Several prognostic models for non-specific low back pain have been described; however, the prognostic factors varied depending on the choice of, for example, the prognostic variables, outcome definition, or the stage of pain (e.g., acute, sub-acute or chronic).[2-4] A recent systematic review focusing on musculoskeletal complaints considered relevant for physical therapists in primary care, reported that the available prediction models are not yet ready to be applied in clinical practice because of their preliminary stage of development.[5] Also, the available models for back pain patients need external validation and impact evaluation before applying them in daily practice.[5] Compared to patients with (sub) acute NSLBP, patients with CNLBP are the least investigated regarding their course and prognosis, especially in relation to the outcomes 'quality of life' and 'global perceived effect' (GPE).[4] Therefore, clinicians and researchers increasingly recognize the importance of such patient-reported outcome measures in the evaluation of the effectiveness of treatment, prognosis or course of CNLBP.[6]

Achieving and maintaining the best possible quality of life is a primary goal of care and several questionnaires are available to measure this item, including the Short Form 36-items Health Survey (SF-36).[7]

With regard to evaluating GPE, the patient can be asked to rate how much their condition (i.e., important aspects of recovery) has improved or deteriorated since some predefined time point.[8]

The present study was designed to investigate the course of and identify prognostic factors (with internal validation) for quality of life and GPE in patients treated for CNLBP.

Methods

Population

Patients were recruited between January 2003 and December 2008 in a prospective cohort study from a multidisciplinary outpatient rehabilitation clinic the Spine & Joint Centre (SJC; Rotterdam, the Netherlands). The Medical Ethics Committee of SJC approved the study protocol and all patients provided informed consent. Details on the study design are described elsewhere.[9] Inclusion criteria were: 1) men and women aged ≥ 18 years; 2) having CNLBP defined as a duration of LBP for ≥ 3 months; 3) previous and unsuccessful treatment in primary and/or secondary care (e.g. physiotherapy). Patient didn't improve in pain, function, work participation and quality of life.

Exclusion criteria were insufficient knowledge of the Dutch language; signs indicating radiculopathy, asymmetric Achilles tendon reflex and/or (passive) straight leg raise test restricted by pain in the lower leg; positive MRI findings for disc herniation; recent (< 6 months) fracture, neoplasm or recent previous surgery (< 6 months) of the lumbar spine, the pelvic girdle, the hip joint, or the femur; specific causes such as ankylosing spondylitis and systemic disease of the locomotor system; and being pregnant or ≤ 6 months post-partum at the moment of consultation.

A total of 2,545 patients [mean age 40.4 (10.9) years; 73.3% women] visited the SJC for an intake consultation, but 785 patients [mean age 41.3 (11.5) years; 70.3% women] decided not to start therapy (e.g., only wanted consultation, diagnose, advise, referred to another specialist, decided later not to come). Data were collected at baseline (n=1,760) and at 2 (n=1,696), 5 (n=1,564) and 12 (n= 965) months-follow-up[10] during regular daily care at the SJC.

Measurements

Outcome measures and defining recovery

To determine the course of quality of life in patients with CNLBP the SF-36 was used and, at 5 months, represented by the two SF-36 domains the Mental Component Scale (SF-36; MCS) and the Physical Component Scale (SF-36; PCS), both ranging from 0-100 (high quality of life).[11-14]

Clinical improvement was measured at 2-, 5- and 12-months follow-up with the GPE score, which consists of a 5-point scale on global change (1=much improved, 2=slightly improved, 3=no change, 4=slightly worsened, 5=much worsened).[15] The two instruments have shown to be reliable and valid.[8,11,12,14,16]

Recovery was defined as a 10% improvement on the MCS or PCS compared to baseline. The scale was dichotomized into 'no improvement in MCS or PCS' and 'improvement in MCS or PCS' based on an increase of 10% at follow-up compared to the baseline value; we considered this to be a clinically relevant difference. A clinically relevant improvement for these scales has not yet been defined, but beside empirical evidence an expert clinical interpretation and judgment is of value. An expert advised us that the most appropriate value for this kind of questionnaire is 10%. Because the changes are smaller than the more common outcomes such as pain and disability. The SF-36 was only followed up to 5 months because this was done electronically at the SJC. The predefined time point for the GPE score[8] was measured following 2 months of therapy at the SJC. In addition, patients judged their own improvement compared with this previous measurement, at 5 and 12-months follow-up. Patients who indicated 'much improved' were coded 'clinically improved' and patients who indicated 'slightly improved', 'no change', 'slightly worsened' or 'much worsened' were coded as 'clinically not improved'.[15]

Potential prognostic factors

The selection of relevant prognostic factors was performed in two steps: 1) the literature on prognosis for CNLBP and quality of life and GPE were reviewed[17], and 2) a clinical group of 8 experts on CNLBP composed a list of 23 of the 47 potential prognostic factors. All factors were retrieved from step 1 (with exception of the factor previous rehabilitation) in combination of the available variables at the SJC. Using the Policy Delphi method (scored on a 4-point Likert scale ranging from 1=very important to 4=not important)[18,19], there were 3 rounds and each time the responses were aggregated, tabulated, summarized, and returned to the experts. In the third round the experts were asked to decide whether to keep or remove the factor from the list, through consensus meeting. The final list consisted of factors that were included by at least 80% consensus. Using these 23 variables, in the analysis we complied with the rule of at least 10 events per variable (which avoids incorrect estimation of variables), we had to restrict the total number of potential prognostic factors.[20] (Box 1) The excluded prognostic factors can be obtained from the first author.

Box 1. *The 23 potential prognostic factors*

Continuous variables

1 Age
2 Duration of back pain in years
3 Present pain intensity (VAS: 0-100 mm)
4 Degree of present fatigue (VAS: 0-100 mm)
5 Quebec Back Pain Disability scale (QBPDS: 0-100)
6 Tampa scale for kinesiophobia (TSK, 17-68)
7 Short-form health survey 36 (SF-36);
Physical Component Scale (PCS) (range 0 ''low quality of life''-100 points)
8 Short-form health survey 36 (SF-36;
Mental Component Scale (MCS) (range 0 ''low quality of life''-100 points)
9 Symptom Checklist 90 (SCL90;item 9; psychoneuroticism)
10 Work participation (0-100%)
11 B200 Isostation (strength back extension in Newton)

Categorical variables

12 Body Mass Index (BMI ≤ 24.9/ 25-29.9/ ≥ 30 kg/m^2)
13 Cause of back pain (accident movement; after physical load; during pregnancy or after delivery; unknown; surgery pelvis/back or HNP)
14 Course of pain in the previous 3 months (stable; increased; decreased)
15 Duration of walking (0-15/ 16-30/ 31-60/ > 61 minutes)
16 Duration of sitting (0-15/ 16-30/ 31-60/ > 61 minutes)
17 Duration of standing (0-15/ 16-30/ 31-60/ > 61 minutes)

Dichotomized variables

18 Gender (female/male)
19 Comorbidity (no versus having one or more co-morbidities)
20 Marital status (being alone versus being married/living with one adult)
21 Level of education (< high school versus ≥ high school/university)
22 Previous rehabilitation treatment (no versus one or more previous rehabilitation treatments)
23 Sickness benefit (no versus all kinds of benefits from the government or employer)

Treatment at the Spine & Joint Centre

The multidisciplinary treatment at the SJC centre used a bio-psychosocial approach consisting of 16 sessions of 3 hours each during a 2-month period (total of 48 hours). Patients were coached by a multidisciplinary team (e.g., a physical therapist, physician, health scientist, psychologist).[9]

Data Analysis

Course of quality of life and GPE

Descriptive analysis was performed to describe the course of quality of life (SF-36; PCS and MCS) and GPE in CNLBP patients according to their characteristics.

The percentage of patients defined as recovered based on a 10% improvement of the MCS and PCS at 2- and 5-months follow-up compared to baseline, was calculated. This was also done for GPE, 'clinically improved' versus 'not clinically improved', at 2-, 5- and 12-months follow-up.

Model development

First, eligible prognostic factors were identified which were highly correlated ($r > 0.8$). This was the case for the B200 Isostation (strength in flexion, extension, lateroflexion, rotation) and the SCL-90 (items 1- 8). Only the B200 extension and the total score item 9 of the SCL-90 were included in the analysis.[21] The continuous factors were checked for linearity using spline regression curves which revealed a non-linear relationship between body mass index (BMI) and the PCS, MCS or GPE. Therefore, BMI was changed into a categorical variable, and also used for the present study and the presented outcomes.

To develop our prognostic model, multivariable logistic regression analysis was performed.[22-25] Regarding missing values, we applied multiple imputation of 5 datasets.[26] Regression equations are used to estimate the missing values. Results of 5 imputed datasets were compared when 40 imputed datasets are used to see if the results would change; this number of 40 was used because in the initial model selection 45.2% of the patients at 12 months (n=795) was missing (loss-to- follow up). Because the results were similar, 5 imputed datasets were used as the primary analysis methods. We also compared the results with complete case analysis (CCA), i.e. all patients with missing data were excluded from the analyses.[27,28]

To develop our prognostic model, multivariable backward logistic regression was performed and initially included 23 potential factors. The variables with the highest p-value were removed one by one, until remaining variables had $p < 0.157$.[23-25,29] The selection of variables was made over all imputed datasets using Rubin's rules.[30] To assess whether the level of significance influenced the final prognostic model for all models, selection of the variables was repeated with p-values of 0.05.

With forward and stepwise selection important variables may be missed in the initial selection phase.[31]

Sensitivity analysis was performed repeating all procedures using GPE as outcome and with a different quality of life cut-off of a 30% improvement on the MCS and PCS with p-values of 0.05 and 0.157.[15]

Performance of the prognostic model

The performance of the model was checked with regard to the goodness of fit (Hosmer-Lemeshow test), the explained variation, and the discriminative ability of the model. The explained variation of the model was estimated by Nagelkerke's R squared. Explained variation is the extent to which the outcome can be predicted by (the predictors in) the model in current dataset(s). The discriminative ability is reflected by the area under the receiver operating characteristic curve (AUC) [range 0.5 (chance) to 1.0 (perfect discrimination)].[32]

Bootstrapping techniques were used to internally validate the models, i.e. to simulate the performance with respect to the explained variance and the AUC in comparable patient datasets.[23,24,33,34]

All analyses were done using SPSS version 18.0 (SPSS Inc., USA) and R software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Population

A total of 1,760 patients [mean age 40.1 (10.6) years; 74.3% women] with CNLBP participated in the study. Of these 1,760 patients,1,696 (96.4%) completed the 2-month multidisciplinary treatment, 1,564 (88.9%) participated in the 5-month follow-up, and 965 (54.8%) completed the 12-month follow-up after start of therapy. Table 1 presents the baseline characteristics of the 1,760 patients and the distribution of the possible prognostic factors.[9]

The baseline characteristics of responders versus nonresponders at 5- and 12-months were similar (data obtained by first author).

Table 1. *Baseline characteristics of 1,760 study participants with chronic non-specific low back pain*[a]

Characteristic	Patients (n=1,608)	Missing values(%)
Number of female patients	1,307(74.3)	0
Age in years: M (SD)	40.1(10.6)	0
Demographic factors		
Low education level	716(40.7)	71(4.0)
Marital status/living with one adult	1,515(86.1)	46(2.6)
Clinical status		
Patients with body mass index > 25	783(44.5)	88(5.0)
Duration of complaints in years: M (SD)	7.7(8.8)	0
Cause reported by patient:		23(1.3)
1 accident/wrong movement	374(21.3)	
2 after physical overload	73(4.1)	
3 during pregnancy or after delivery	586(33.3)	
4 surgery pelvis/back or after HNP	32(1.8)	
5 unknown	672(38.2)	
Previous revalidation program	186(10.6)	101(5.7)
Comorbidity	275(15.6)	88(5.0)
Pain intensity LBP (VAS in mm): M (SD)		
1 present pain intensity	55.5(23.0)	5(0.3)
Course of pain intensity due to CNLBP in the previous 3 months		52(3.0)
1 stable pain intensity	865(49.1)	
2 increased pain intensity	723(41.1)	
3 decreased pain intensity	120(6.8)	
Degree of fatigue LBP (VAS in mm): M (SD)		
1 present fatigue	56.5(26.6)	118(6.7)
Disability (QBPDS): M (SD)	51.7(15.6)	8(0.5)
Psychological factors		
Fear avoidance (TSK): M (SD)	36.7(7.3)	50(2.8)
SCL90 item 9 M(SD)	149.3(39.7)	227(12.9)
SF-36 (health-related quality of life)		
PCS	31.8(7.1)	493(28.0)
MCS	46.5(10.3)	493(28.0)
Work-related factors		
Sickness benefit	924(52.5)	353(20.1)
Work participation		161(9.1)
1 100% working	391(22.2)	
2 0-99% working	1,059(60.2)	
3 not working*	149(8.5)	
Physical examination		
ADL function – duration > 31 min without pain increase		
1 walking	410(23.3)	10(0.6)
2 sitting	432(24.5)	13(0.7)
3 standing	106(6.1)	9(0.5)
B200 Isostation (strength) (Newton): M (SD)		
1 extension	81.6(45.8)	107(6.1)

[a] *Values are numbers (percentages) unless stated otherwise in the entire data set of 1760 patients. M = mean; SD = standard deviation; CNLBP = chronic non-specific low back pain; VAS = Visual analogue scale; QBPDS = Quebec Back Pain Disability Scale; TSK = Tampa Scale Kinesiophobia ; SCL-90 (item 9)= Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary; ADL= activities of daily living. Missing values ranged from 0.5% (n=9) to 28% (n=493). *''not working'' were patients not working at this moment due to seeking new work, or not seeking work because they have family care responsibilities or are retired.*

Course and prognostic models of quality of life

Course at 2- and 5-months

At 2- and 5-months follow-up the mean MCS improved slightly from 46.6 (SD 10.3) at baseline to 49.2 (SD 9.4) at 2 months and to 50.4 (SD 9.8) at 5 months. The mean PCS also improved from 31.9 (SD 7.1) at baseline to 40.7 (SD 8.2) at 2 months and to 42.1 (SD 10.1) at 5 months. At 5 months, a 10% improvement was reported by 20.6% of the patients with regard to the MCS score and by 76.3% with regard to the PCS score (Table 2).

Table 2. *Course of quality of life (SF-36) and global perceived effect (GPE) in patients with chronic non-specific low back pain at 2-, 5- and 12-month follow-ups*

Quality of life (SF-36)	Baseline (n=1,267)	2 months (n=1,252)	5 months (n=1,013)	12 months
PCS; mean (SD)	31.9 (SD 7.1)	40.7 (SD 8.2)	42.1 (SD 10.1)	
MCS ; mean (SD)	46.6 (SD 10.3)	49.2 (SD 9.4)	50.4 (SD 9.8)	
10% improvement in				
PCS		76.6%	76.3%	
MCS		39.6%	20.6%	
Global Perceived Effect	Baseline	2 months	5 months (n=1,564)	12 months (n=965)
1 much improved		45.1%	53.0%	60.3%
2 slightly improved		44.1%	32.1%	19.1%
3 no change		7.4%	9.3%	10.8%
4 slightly worsened		3.1%	3.9%	5.7%
5 much worsened		0.3%	1.8%	4.1%
Clinical improvement		45.1%	53.0%	60.3%

PCS= Physical Component Scale of the Short Form-36; MCS= Mental Component Scale of the Short-Form 36; mean (SD = standard deviation), n = number of patients.

Prognostic factors for improved quality of life at 5-months follow-up

Table 3 shows the associations between potential prognostic factors and PCS and MCS at 5-months follow-up.

The outcome of 10% improvement on the SF-36 PCS was most strongly associated with the following baseline scores: a BMI score ≥ 30 kg/m^2 (OR 1.56, 95% CI 0.96-2.53), receiving sickness benefit (OR 1.90, 95% CI 1.08-3.34), a higher level of work participation (OR 2.03, 95% CI 0.93-4.41), and 16-30 min duration of walking (OR 1.78, 95% CI 1.08-2.97). The AUC of this model was 0.69 and the explained variance was 11%.

The factors most strongly associated with a 10% improvement on the MCS score were being female (OR 0.70, 95% CI 0.43-1.113) and having a lower MCS score at baseline (OR 0.82, 95% CI 0.79-0.84). The AUC of this model was 0.88 and the explained variance was 44%.

With regard to internal validation of the models, for PCS the explained variance at 5-months follow-up was 12% with an AUC of 0.69; for MCS these figures were 44% and 0.88, respectively.

Table 3. *Multivariable models of prognostic factors for 10% improvement in quality of life in patients with chronic non-specific low back pain at 5 months*

Outcome and domains	5-months follow-up		
Outcome Physical Component Scale	OR	95% CI	p-value
Patient characteristics			
Age in years	0.98	0.97-0.99	< 0.001
BMI ≥ 25-29.9 kg/m^2	1.14	0.87-1.50	0.334*
BMI ≥ 30 kg/m^2	1.56	0.96-2.53	0.07
Psychological factors			
SF-36 PCS	0.94	0.92-0.96	< 0.001
SF-36 MCS	1.03	1.01-1.05	0.01
SCL-90 (item 9)	1.00	0.99-1.01	0.14
Work-related factors			
Sickness benefit(no/yes)	1.90	1.08-3.34	0.03
Work participation	2.03	0.93-4.41	0.07
Physical examination			
Duration walking 1 (0-15 min)	1.19	0.75-1.89	0.419*
Duration walking 2 (16-30 min)	1.78	1.08-2.97	0.03
Duration walking 3 (31-45 min)	1.68	0.77-3.69	0.17*
Outcome Mental Component Scale	OR	95% CI	p-value
Patient characteristics			
Gender (female/male)	0.70	0.43-1.13	0.13
Psychological factors			
SF-36 PCS	1.03	1.00-1.07	0.05
SF-36 MCS	0.82	0.79-0.84	< 0.001
SCL-90 (item 9)	0.99	0.99-1.00	< 0.001

95% CI= 95% confidence interval, OR = odds ratio, an OR > 1 reflects a higher probability of 10% recovery for the outcome PCS and MCS and an OR < 1 a lower probability of 10% recovery for the outcome back pain intensity, compared to the reference category. OR estimated after multiple imputation (n=5 datasets) with p-value of 0.157. SCL-90 (item 9)= Symptom Checklist; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary. The variable body mass index (BMI) is a category value of 3 (18-24.9 kg/m^2; ≥ 25-29.9 kg/m^2; ≥ 30 kg/m^2); the variable duration walking is a category value of 4 (0-15;16-30;31-45;60>).

Course and prognostic models of GPE

Course at 5- and 12-months follow-up

At 5- and 12-months follow-up, clinical improvement was reported by 53% and 60.3% of the patients, respectively. In addition, at 5- and 12-months follow-up, 'no change to much worsened' was reported by 15% and 20.6% of the patients, respectively (Table 2).

Prognostic factors for GPE at 5- and 12-months follow-up

Table 4 shows associations between potential prognostic from the predefined time point (i.e., after 2 months of therapy at SJC) and GPE of the patients at 5- and 12- months follow-up.

Being married (OR 1.39, 95% CI 1.00-1.91), decrease of pain intensity in the last 3 months (OR 2.07, 95% CI 1.23-3.48), receiving sickness benefit (OR 1.61, 95% CI 0.96-2.69) and a higher work participation (OR 1.92, 95% CI 1.03-3.59) were the strongest factors associated with clinical improvement on the GPE scale at 5-months follow-up. At 12-months the following factors showed the strongest associations: being female (OR 0.63, 95% CI 0.47-0.84), being married (OR 1.51, 95% CI 1.03-2.21), higher work participation at baseline (OR 1.65, 95% CI 1.18-2.29) and duration of walking 16-31 min at baseline (OR 1.58, 95% CI 0.88-2.82). The explained variance and AUC for 5 and 12 months were 11% and 0.66, and 9% and 0.65, respectively. The internal validation showed similar results in the GPE for explained variance and AUC.

Table 4. *Multivariable models of prognostic factors for absolute recovery in chronic non-specific low back pain, global perceived effect (GPE) at 5- and 12-month follow-ups*

Outcome and domains	5-months follow-up			12-months follow-up		
Outcome GPE	OR	95% CI	p-value	OR	95% CI	p-value
Patient characteristics						
Age in years	0.97	0.96-0.99	< 0.001	0.98	0.97-0.99	0.002
Gender (female/male)				0.63	0.47-0.84	0.002
Married/being with one adult (no/yes)	1.39	1.00-1.91	0.05	1.51	1.03-2.21	0.03
Clinical status						
Duration of complaints	0.99	0.97-1.00	0.05	0.98	0.97-0.99	0.02
Course of pain intensity due to CNLBP in the previous 3 months (increase of pain)	1.05	0.84-1.30	0.681*			
Course of pain intensity due to CNLBP in the previous 3 months (decrease of pain)	2.07	1.23-3.48	0.007			
Back pain intensity (VAS)	1.00	0.99-1.00	0.09	0.99	0.98-0.99	< 0.001
Disability (QBPDS)	1.01	1.00-1.02	0.01			
Psychological factors						
TSK	0.97	0.96-0.99	0.005			
SF-36 PCS	1.05	1.03-1.07	< 0.001			
Sf-36 MCS	1.02	1.00-1.03	< 0.001			
Work-related factors						
Sickness benefits (no/yes)	1.61	0.96-2.69	0.07			
Work participation	1.92	1.03-3.59	0.04	1.65	1.18-2.29	0.005
Physical Examination						
B200 Isostation extension	1.00	0.99-1.00	0.08			
Duration walking 1 (0-15 min)				1.00	0.74-1.36	0.99*
Duration walking 2 (16-30 min)				1.58	0.88-2.82	0.11
Duration walking 3 (31-45 min)				1.32	0.89-1.96	0.16

95%-CI= 95% confidence interval, OR = odds ratio, OR estimated after multiple imputation (n=5 datasets) with p-value of 0.157. VAS= Visual Analog Scale; QBPDS = Quebec Pain Disability Scale; SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary. The variable course of pain intensity due to CNLBP in the previous 3 months is a category variable, 1) increase, 2) decrease and 3) stable of pain intensity; the variable duration walking is a category value of 4 (0-15;16-30;31-45;60>)

Sensitivity analysis regarding quality of life and GPE

Repeating the analysis with p-values of 0.05 or 0.157, and using CCA or 5 or 40 imputated datasets, resulted in similar prognostic factors for a 10% improvement in the PCS, MCS and GPE-score at 5-months follow-up. At 12-months, younger follow-up age, less pain intensity at baseline, higher work participation or shorter duration of complaints were often related to GPE in the different models. The explained variance, AUC and internal validation were similar to earlier findings.

Discussion

In the present study, a main finding is the sustained 10% improvement on the PCS (76.3% of the population) up to 5-months and on GPE (60.3%) up to 12-months. For MCS this 10% improvement is slightly less (20.6%) at 5-months, but a mean of 50 (SD of 10) represents normal health and function.[14] Some patients reported no improvement on GPE at 5- and 12-months follow-up (15% and 20.6%, respectively).

The present study shows that improvement in quality of life (on SF-36 MCS) at 5- months follow-up was associated with patients' characteristics and psychological factors. At 5 months, improvement on quality of life (on SF-36 PCS) and GPE was associated with patients' characteristics, physical examination, work-related factors and psychological factors. For GPE, clinical status was also associated with improvement.

At 12-months follow-up GPE was associated with patients' characteristics, clinical status, physical examination and work-related factors. The sensitivity analyses showed overall similarity for the prognostic factors. The prognostic models provide additional information to present a more realistic expectation regarding outcome. However, development of a prognostic model does not involve investigating the causal associations between individual prognostic factors and outcome.

Comparison of the present results with earlier studies is limited, because our systematic review identified only 3 low-quality studies addressing this topic.[4] For the outcome SF-36 PCS, Keeley et al. had a 6-months follow-up with a mean SF-36 PCS score of 34.9 (SD 10.9) compared with a baseline score of 33.3 (SD 10; n=93).[35] The present study showed a greater improvement on the PCS score, i.e. from 31.9 (SD 7.1) at baseline to 42.1 (SD 10.1) at 5 months. The difference in results might be due to differences in study characteristics; e.g. patients in the study of Keeley et al. did not follow a therapy program but could contact their healthcare provider when needed[35]; the authors concluded that an intervention targeting these psychosocial variables in patients, may lead to improved quality of life and reduction of healthcare costs.[35] A study by van der Hulst et al.[36] from the same systematic review on SF-36 PCS and MCS, showed more similarity with the present study at 6-months follow-up.

Their patients with CNLBP experienced (on average) better health-related quality of life than at baseline, regardless of the type of treatment [Roessingh Back Rehabilitation Program (RBRP) vs. usual care]. At follow-up the RBRP (7-week program) resulted in a PCS score of 37 (SD 9) and an MCS score of 51 (SD 9) compared with baseline scores of 31 (SD 7) and 49 (SD 10), respectively.[36]

In relationship to the course of GPE, our systematic review[4] found only one study, which reported that 29% of the non-surgical group assessed themselves as improved at 2-year follow-up.[37] In contrast, 60.3% of our patients reported clinical improvement on the GPE scale at 12-months follow-up.

In the final prognostic model on PCS reported by Keeley et al.[35], the Hospital Anxiety and Depression Scale (HADS) total score and back-pain related social stress, continued to make a significant contribution to the model (R2 = 0.72; incidence rate ratio around 1.00). In the present study, the psychological factors [SCL-90 (item 9) and MCS; OR around 1.00] were included, as were other factors with a strong association. In both studies, the psycho-social results had a low association; further research on these items is necessary.

In the present study no association was found for the factor 'fear avoidance beliefs' and the outcome PCS. In two of the studies in our systematic review[4] conflicting evidence was found for their 8-week[36] and 6-month[35,36] follow-up, whereas the 6-month follow-up data of Keeley et al.[35] are similar to those in the present study. The discrepancy between these results may be due to differences in characteristics between the two studies, including a smaller patient population (n < 200), differences concerning treatment/no treatment, in the length of follow-up (8 weeks), and in the included prognostic factors. In the 2-months therapy at the SJC and in the 7-week RBRP program of van der Hulst et al.[36], fear of avoidance beliefs was a part of the program but yielded differing results, possibly due to other aspects of the therapy program. In van der Hulst's study, presence at work predicted improvement for the PCS at 6-months follow-up[36], which is in line with our results at 5-months follow-up. This might be explained by the fact that people at work are generally healthier and more physically active, which may be related to greater physical wellbeing. However, because this comparison is with only one study, more research is needed on this topic. Also, in van der Hulst's study, whereas higher depression scores (SCL-90-dep) predicted deterioration on the MCS on the short and long-term follow-up regardless of treatment[36], this was in contrast to our results.

For the outcome GPE only one study was found[4], reporting that increased pre-treatment depressive symptoms measured with the Zagazig Depression Scale predicted improvement of the GPE score in a non-surgical group of CNLBP patients[37], We found no association with the SCL-90 (item 9) in the final model at 5- and 12-months follow-up.

The present study benefited from a large sample size (n=1,760), prospective design, and patients' self-report. Although there are many ways to build a prognostic model (including internal validation), we followed the optimal way as reported in the literature.[38]

We used the rule of 10 events per variable to minimize the risk of bias due to overfitting.

The outcome quality of life and GPE were two of the 5 outcomes (back pain intensity, disability due back pain, work participation, quality of life and patients' perceived recovery) measured in this prospective cohort study. The choice for these current outcomes is because this is important to the patient and also only a few other studies are known.

Of all patients, 90.2% had stable or increased low back pain intensity in the 3 months prior to intake.[10] The duration of complaints in our study population was on average 7.7 years. During the 12 months there we those patients that recovered from back pain, those who experience it off and on and those who have it most of the time.[39-41] Recent studies[39,40] reports that most patients with back pain appear to follow a particular pain trajectory over longer time periods, and do not have frequently recurring of widely fluctuating patterns. It can be that a particular pain trajectory will have certain clinical characteristics. This could influence which prognostic factor is important as also the effect in rehabilitation.[39]

The present study also has some limitations. First, despite the large sample size, at baseline there were missing values (0.5-28%). Also, at 12-months follow-up only 54.5% of the patients could be compared with the baseline measurements. Our study gathered the data at the rehabilitation centre SJC during daily practice and at 12 months this was done postal. The SF-36 (28% missing values at the baseline) is collected electronically and separately from the other data at the start of therapy by a therapist. The general practitioner (GP) asked at baseline which kind of sickness benefit (20%) a patient had. Sometimes this was forgotten. Other reasons could be that Dutch was not the first language of the patient maybe not all the questions were understood, or an incomplete questionnaire was retrieved. Loss to follow-up (i.e., failure to return the follow-up questionnaires) occurred for various reasons, including vacation, envelope not stamped, recovered from CNLBP, did not find it necessary, starting another intervention, etc. No reminder was send to patient. We assume that the missing values occurred at random, which is not uncommon with a long-term follow-up. Also, we used imputation of data (multiple imputation techniques); however, this is reported to be a valid method to deal with missing values[28] and the sensitivity analyses yielded similar results.

We cannot demonstrate the influence of the given cognitive behaviour therapy with supervised exercises, educational and multi-disciplinary treatment. Only, that this is one of the most common intervention for CNLBP in Dutch rehabilitation centres and two Cochrane reviews[42,43] provided evidence of a greater improvement on the short term than other treatments.

For the present study, although we chose for a cut-off point of 10% improvement on the SF-36 PCS and MCS, there was little difference in identifying prognostic factors when a 30% improvement was used.

A 30% improvement is a more commonly used criteria in CNLBP especially for the outcome pain and disability[15,44]; however, the problem remains that patients close to, but on opposite sides of the cut-off point, are characterized as being very different rather than very similar. Also, although the currently available GPE scale has the option 'completely recovered'[45], this was not yet in use in the SJC when the data were retrieved. This latter outcome measure is often dichotomized because it is easier for interpretation by clinicians and patients, albeit with the risk of losing some information.[46] Because patients have difficulty taking their baseline status into account when scoring the GPE scale[8], this item was compared with the end of therapy at the SJC.

Further research should focus on (external) validation of the presented prognostic models with appropriate study methodology, rather than developing new ones. With further testing the practical value of the models can be properly established.[23] The impact for the clinician is that the current thought suggest a more complex interaction between factors rather than singular prognostic factors that influence the patient through time. There is clearly a need to investigate how prognostic factors work together in their usefulness and feasibility in clinical practice.

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CHAPTER 8

General Discussion

The overall aim of this thesis was to: 1) review the literature to identify prognostic factors for the following 5 outcomes: low back pain intensity, disability, return to work, quality of life, and patients' perceived recovery with chronic non-specific low back pain on the short-term (≥ 6 months) and long-term (> 6 months) follow-up; 2) assess the characteristics and clinical course for patients with chronic non-specific low back pain treated in a tertiary rehabilitation centre with a 12-month follow-up period, and 3) identify the prognostic factors for recovery (including internal validation of the prognostic models) of patients treated in a tertiary rehabilitation centre for the outcomes: low back pain intensity, low-back-pain-specific disability, work participation, quality of life and patients' perceived recovery with chronic non-specific low back pain.

A substantial part of this thesis is based on a prospective cohort study performed among patients from a multidisciplinary outpatient rehabilitation centre the 'Spine & Joint Centre' (SJC) in Rotterdam, the Netherlands. All participating patients (n=1,760) were recruited between January 2003 and December 2008 and were evaluated by means of questionnaires and physical examinations at baseline, during the 2-month therapy program and at 5-months after the start of the SJC therapy program (2 months twice a week at the SJC + 3 months self-supporting activity). The 12-month follow-up measurement was performed by means of a postal questionnaires sent to the patients. The baseline characteristics of the included patients (Chapter 3) were similar to those of patients in other studies on chronic non-specific low back pain.[1, 2]

In our study, recovery was assessed using various outcome measures and operationalised according to two definitions: 1) a 30% improvement compared with baseline scores for the outcomes back pain intensity, disability, work participation and quality of life (SF-36; 10% improvement)[3-5] and 2) an 'absolute recovery' as defined using a Visual Analogue Scale (VAS) score of pain intensity ≤ 10 mm, disability as assessed by the Quebec Back Pain Disability Scale (QBPDS) score of

≤ 20 points, work participation (0-100% working) of ≥ 90% at follow-up, and global perceived effect (GPE) using a 5-point scale dichotomised into 'clinically improved' vs. 'clinically not improved'.[4,6-9] The therapy protocol at the rehabilitation centre used a bio-psychosocial approach to stimulate patients to adopt adequate (movement) behaviour aimed at physical and functional recovery (see Chapter 3).[2] Prognostic models, including internal validation of the 5 outcomes of interest, were developed for both the 5 and the 12-month follow-up.[10-12]

Clinical course

This section presents the results of the clinical course of chronic non-specific low back pain for both the percentage of improvement and the absolute recovery. In addition, for each of the 5 outcomes, comparisons with other studies are discussed.

The clinical course based on the 5 outcomes described in Chapters 4-7 showed a slight improvement for all outcomes during the 1-year period after treatment (Table 1). On average, about 60% of the patients reported a 30% improvement in back pain intensity, disability and work participation at their 12-month follow-up. Patients also reported a ≥ 60% improvement in quality of life (SF-36), and an improvement on the Physical Component Scale (PCS) at 5-months for the outcome '10% improvement of recovery'. On the Mental Component Scale (MCS) of the SF-36, 21% of the patients reported a 10% improvement at 5-months. However, when recovery was defined with a cut-off percentage [pain intensity ≤ 10 mm, disability ≤ 20 points, work participation (0-100% working) of ≥ 90% at follow-up, and GPE on a 5-point scale dichotomized into 'clinically improved' vs. clinically not improved'[4,6-9]] the results were lower, i.e. 29%, 38%, 52% and 60% for back pain intensity, disability, work participation, and clinical improvement on the GPE, respectively.

With regard to comparison with other studies, many used a different methodology, or were population-based investigating the general population, or a primary care or another type of group. Moreover, they often used a different cut-off point to classify patients as being 'recovered' and used different points of measurement over time to evaluate patient recovery.[13-19] Although all these differences hamper a direct comparison, some general comparisons can be made.

The results of our study on the clinical course of back pain intensity (Chapter 4) and on disability (Chapter 5) showed some similarities compared with earlier studies.[13-21] In the study of Costa et al. (2009), of the 259 patients who had not recovered (not pain-free, still had disability from back pain, and had not returned to work in their previous capacity for 30 consecutive days), on entry to that study 47% had recovered after 1 year.[22] Results of two systematic reviews showed that ≤ 50% of the patients had recovered from low back pain within 1 year.[21,23] Studies with ≥ 1-year follow-up (such as a Dutch population study that measured three times over a 10-year period) found that 30% of the population were free of back pain at

all follow-up points (low back pain was considered long standing if persisting for > 3 months).[24] One Swiss study with a 5-year follow-up reported similar results, i.e. 35% (low back pain problems at least once a month in the last 12 months) pain free at follow-up.[25] Another study by Enthoven et al. (2004) showed that 52% of chronic and recurrent low back pain patients reported pain (VAS > 10 mm) and back-related disability (Oswestry, > 10%) at the 1 and 5-year follow-up.[16]

In the present study, an interesting finding was that there was more improvement in disability than in pain intensity. This finding is consistent with results from earlier trials[26, 27] and a systematic review[28] in which patients received a program on cognitive behaviour principles. Grotle et al. (2010) found only a moderate change in disability after 1 year (25% reduction) in patients with chronic low back pain.[29] However, a recent meta-analysis found a greater change in pain than in disability over 1 year[30]; however, the studies included in the latter review did not include exercise programs with cognitive behavioural principles, which may explain the differences in findings.

Our study also showed that, directly after the 2-month multidisciplinary cognitive behaviour therapy at the SJC rehabilitation centre, patients experienced the greatest change in improvement post-baseline in all outcomes compared with the 5 and 12-month follow-up. At the 5-month follow-up in which the patients followed a 3-month self-management program[2] the differences compared with a 2-month program were relatively small. A similar pattern was reported during the first 4-6 weeks in a recent meta-analysis[30] and in other studies[13,16,19] describing a slowly advancing reduction in average pain and disability between 6 and 52 weeks.

Our study population received therapy aimed at physical/functional recovery, which may partly explain the positive increase in work participation (Chapter 6). A systematic review by Guzman et al. (2002) provides evidence that intensive multidisciplinary bio-psycho-social rehabilitation with a functional restoration approach, improves pain and function in patients with chronic non-specific low back pain and increases the ability to work.[28] Social disadvantage (e.g., income, health care access, immigration status, language barriers), social factors at work (e.g. supervisor & co-workers support, job stress and burn-out), spousal support and family conflict may increase the time period before some patients are able to return to work.[31] Thus, many factors can interfere with the course of improving patients' work participation. For sub-acute low back pain there is moderate evidence showing that multidisciplinary rehabilitation (which includes a workplace visit or a more comprehensive occupation healthcare intervention) results in patients returning to work faster.[32] A work place visit might be a positive addition to the program of the SJC rehabilitation centre.

For the course of quality of life (SF-36 PCS, MCS) and GPE (Chapter 7) fewer studies are available with which to compare our results.[8,16,33-35] Our study showed more improvement on the PCS of the SF-36 at the 5-month follow-up compared with other studies.[33,34] This lack of consistency may be the result of differences in study methods[33,34]; for instance, in other studies patients did not follow a therapy program, but could contact their clinicians if required. The MCS of the SF-36 showed more similarity with an earlier study that also followed patients after a multidisciplinary therapy for 6 months.[35]

In relationship to the course of GPE, in our systematic review[1] only one study reported that, in a non-surgical group of chronic low back pain patients, 29% assessed themselves as improved at the 2-year follow-up. Other studies also showed improvement from the patient's perspective over a 12-month period; however, because they used other scales and different cut-off points comparison is difficult.[36,37] In our study we found that 60% of the patients reported a clinically relevant improvement at the 12-month follow-up.

In summary, the clinical course of patients with chronic non-specific low back pain who did not recover during primary and secondary care seems to improve after a rehabilitation program, with success rates up to 60% at 12-months follow-up depending on the definition of recovery and the type of outcome measure used.

Prognostic models

Knowledge on prognostic factors is important to help identify patients who are more likely to recover from chronic non-specific low back pain following multidisciplinary cognitive behaviour treatment. In essence, prognostic factors based on a single outcome measure may not fully represent all aspects of recovery from a multidimensional condition, such as chronic non-specific low back pain.[38]

Our earlier systematic review emphasises that evidence on the prognostic factors for recovery in patients with chronic non-specific low back pain is not only scarce but also inconclusive.[1] In our prospective cohort study, prognostic factors for the 5 outcomes were found (Chapters 4-7). These findings proved to be similar to those of earlier studies by others, but also provided new insight into the prognosis in patients with chronic non-specific low back pain treated in multidisciplinary tertiary care. This is a first initiative to collect and analyse data for 5 outcome measurements in tertiary care, for patients in whom primary and secondary care failed to lead to recovery of the patient's complaints. In various previous studies, certain prognostic factors had not been studied and the outcome of work participation had not been evaluated on the short-term follow-up.

Chapters 4-7 presented the multiple prognostic models; in each article, the factors, limitations and influence of these models are described. Below, for each domain, we describe the prognostic factors that most frequently occurred in the results (e.g., patients' characteristics) and in the outcome (e.g., work participation).

Table 1. *Results of the clinical course of chronic non-specific low back pain over a 12- month follow-up period (data are mean and SD or % as indicated)*[a]

Clinical course	Baseline (n=1,752)	2 months (n=1,696)	5 months (n=1,564)	12 months (n=965)
Back pain intensity (VAS)				
Back pain intensity: mean (SD)	55.5 (SD 23.0)	37.0 (SD 23.8)	35.3 (SD 26.1)	32.3 (SD 26.9)
30% improvement in back pain intensity		53.8%	55.2%	60.5%
Absolute recovery on pain score (≤ 10 points)	3.8%	13.7%	19.8%	28.6%
Disability (QBPDS)				
Back Pain Disability: mean (SD)	51.7 (15.6)	31.7 (15.2)	31.1 (18.2)	29.1 (20.0)
30% improvement on back pain disability		62.6%	61.3%	63.4%
Absolute recovery on disability score (≤ 20 points)	2.6%	24.1%	30.9%	38.3%
Work participation *				
Work participation: mean (SD)	38.3 (SD 43.1)		73.4 (SD 44.9)	81.7 (SD 52.9)
30% improvement on work participation			30.3%	60.5%
Absolute recovery on work participation (90%)	25.4%		43.2%	52.0%
Quality of Life (Short Form-36)				
Physical Component Scale (PCS): mean (SD)	31.9 (SD 7.1)	40.7 (SD 8.2)	42.1 (SD 10.1)	
Mental Component Scale (MCS): mean (SD)	46.6 (SD 10.3)	49.2 (SD 9.4)	50.4 (SD 9.8)	
10% improvement on the PCS		76.6%	76.3%	
10% improvement on the MCS		39.6%	20.6%	
Global perceived effect (GPE 5-point scale)				
Clinical improvement GPE		45.1%	53.0%	60.3%
1 much improved		45.1%	53.0%	60.3%
2 slightly improved		44.1%	32.1%	19.1%
3 no change		7.4%	9.3%	10.8%
4 slightly worsened		3.1%	3.9%	5.7%
5 much worsened		0.3%	1.8%	4.1%

[a] *n= number of patients in analysis ;SD= standard deviation; VAS = Visual analogue scale, 0-100, 0=no pain; QBPDS = Quebec Back Pain Disability Scale, range 0-100, higher score indicates more disability; work participation (0-100%) current work hours/ contracted hours; * included those patients with paid work (n= 1608); SF-36 = Short Form; PCS = Physical Component Summary; MCS = Mental Component Summary range 0-100, higher score indicates better quality of life; Missing values ranged from 0.5% to 35.2%.*

Patients' characteristics

A lower age [OR 0.98 (CI 95% 0.96-0.99)] was shown to provide a better chance of recovery during the 12-month follow-up for the outcome back pain intensity (Chapter 4), low-back-pain-specific disability (Chapter 5), patients' perceived recovery (Chapter 7), as well as for the outcome PCS on the SF-36 (Chapter 7) at 5 months, and work participation (Chapter 6) at 12-month follow-up.

Our systematic review consistently revealed no association between age, and back pain intensity and low-back-pain-specific disability; also, work participation showed conflicting evidence with regard to age on the long term (> 6 months).[1] In summary, in all our multivariable models the course seems to be less favourable for older than for younger patients. The difference between these two groups probably lies in the patient's overall health, different life stages, and the chance of having co-morbidities[39] and/or less compliance with the treatment, because changes in cognition and behaviour may become more challenging as patients become older. Neurophysiological musculoskeletal changes or genetic factors[39], a normal part of the aging process, may imply that a patient needs more time or another type of treatment to recover from chronic non-specific low back pain. A recent study showed that back pain had a greater impact with increasing older age.[40]

Being female [OR 0.72 (CI 95% 0.49-1.07)] was positive for the 5-month course when using the percentage of improvement for the outcome back pain intensity and the MCS on the SF-36. The same results were found for the outcome of back pain intensity and the GPE score of the patients at 12 months. Absolute recovery on work participation was associated with being male [OR 1.79 (CI 95% 1.25-2.55)]; this might be because, in Dutch society, men traditionally earn the most wages for the family and it is less acceptable to work fewer hours. Other results from our systematic review provide consistent evidence for no association on the short term (≤ 6 months) and conflicting evidence on the long term (> 6 months) follow-up for back pain intensity, low-back-pain-specific disability and the outcome work participation.[1] Most low back pain studies report that older age and female gender are risk factors for poorer outcomes with acute and/or chronic low back pain, whereas some studies report no such effects.[1,31]

Being married or living with another adult [OR 1.60 (CI 95% 0.99-2.57)] can provide social support for patients during their rehabilitation process, especially when they are involved in the program, as was the case with our cohort study. For the 30% improvement, this had a positive influence at 5 months for disability and for absolute recovery, GPE, and work participation. During the 12-month follow-up the outcome of back pain intensity was also added to the model, whereas for work participation there was no association. We have no explanation as to why there is no association between being married and work participation. There is some evidence for detrimental consequences of low back pain on marital satisfaction, partner emotions and relationship quality[41]; on the other hand, beneficial effects are reported of spousal support and social interaction with other patients on low back pain coping and function for the outcome 'pain and disability'.[42,43]

Clinical status at baseline

Within the domain clinical status, the prognostic factors most frequently present in the different models for the outcome measures (except for the outcome quality of life) were the baseline scores of self-reported back pain intensity and low-back-

pain-specific disability. Due to the low value of association (OR around 1), it seems that the choice of outcome definition of the minimal clinically important changes (MCICs) caused the difference. In our systematic review, self-reported pain at baseline had no association with back pain intensity and disability at 12 months, and there was limited evidence for a positive effect if a patient had less self-reported pain at baseline for the outcome of work participation.[1] In our models, less back pain intensity at baseline (6 models) shows a trend of an increased positive influence to recover, than more back pain intensity at baseline (2 models). Pain reduction is not a primary outcome measurement in most of the cognitive behaviour treatments, but seemed to play a role in the prognosis for recovery in these patients. Patients may have different types of pain, e.g. some have pain consistently, whereas others experience pain sporadically throughout their life.[39] Whether these differences are due to different levels of vulnerability (e.g., genetic and environmental factors) or to a cumulative impact of the pain experience remains to be seen.[39] Two studies performed in a primary care setting found that patients' belief about their back pain is an important and robust prognostic factor on both the short and long term, together with pain intensity, depression and compensation claim status.[44,45] The question remains whether we as clinicians should take this into account during the rehabilitation program, by more frequently informing patients about the mechanism(s) of recovery for chronic non-specific low back pain.
Furthermore, more consistent associations have been found between less back pain and more physical activity in the elderly than in the younger population.[46]

Psychological factors

Overall, our study showed that over the course of 12-months the factor 'kinesiophobia' was not associated with the outcomes of interest. Our systematic review found conflicting evidence for the outcome of back pain intensity and low-back-pain-specific disability at short-term follow-up.[1] For the long-term follow-up, the PCS and MCS on the SF-36 also demonstrated conflicting evidence. Only the outcome low-back-pain-specific disability showed consistent evidence of no association with kinesiophobia on the long-term follow-up. However, some of the studies in our systematic review were of low methodological quality and the value of the prognostic factor was not always convincing. A recent study among acute and chronic low back pain patients in primary care reported the same results as found in our cohort study, i.e. no association with the outcome back pain and disability.[44] Also catastrophising, passive coping, anxiety and depression were included in their model, but showed no association on the short term (6 months) and long term (5 years).[44] The lack of prognostic value of the factor 'fear avoidance' is interesting, because this is considered to be an important aspect of cognitive behaviour therapy. This probably explains why a small subgroup of acute low back pain patients develops a chronic pain problem.[47]

However, this factor may be less important (or overrated) for patients with chronic non-specific low back pain. Another explanation may be that, nowadays, most patients already receive several therapy sessions, with the fear-avoidance model as a basis for intervention, applying operant conditioning and graded activity in primary/secondary care before starting a tertiary care rehabilitation process. Therefore, perhaps only a small majority of patients with chronic non-specific low back will experience fear, catastrophising and/or anxiety during a relapse of intensified pain intensity or functional disability and are not able to cope, whereas others can.[47] We also have to take into account the inconsistent and weak methodological values in the other studies, implying that the clinical value may be overrated. This raises the question of how the fear-avoidance model might best be tackled within the treatment, or whether there is some acceptance of chronic pain by patients in their daily life.

A higher baseline score for quality of life [OR for PCS 1.07 (CI 95% 1.03-1.11) and OR for MCS 1.02 (CI 95% 1.01-1.04)] increases the chance of recovery for patients over a 12-month period, except for the outcome work participation and the GPE; however, the ORs were small. Although there is no explanation for this in the literature, the answer might depend on the definition of work participation used. We did not measure other qualitative values, such as willingness to work, enjoyment in one's work, or the desire to return to work. For the GPE a recent study concluded that the rating of the GPE scale is strongly influenced by the patient's current health status.[48] Overall, the mechanisms behind the relationships between back pain and general physical/mental health are poorly understood, but appear to be present throughout life.[39]

Work-related factors

For back pain intensity and low-back-pain-specific disability, the factor 'work participation' at baseline [OR 1.27 (CI 95% 0.93-1.73)] showed the tendency: "the more one is working at baseline, the better it is for one's recovery" at 5 months follow-up. However, at 12 months there was no such association. Our systematic review found conflicting evidence for this association with back pain intensity or disability on the long term (> 6 months).[1] All the studies included in our review were of low methodological quality. If we add these results to our findings on the clinical course and our prognostic models on absolute recovery for work participation, GPE and a 10% improvement on the PCS for quality of life, this shows that being at work is important for recovery at 5 and 12-month follow-up. This might be because people who are working are generally healthier, experience social support and are more physically active, all of which may be related to greater physical wellbeing and an increased chance to recover.[49] The factors of pain and disability are often related to returning to work[1,50] but, on our findings, are inconclusive. The challenge remains for the practitioner to advise their patients to continue working and also to even extend their working hours over time, despite the experienced pain and disability.

General comments on course and prognosis

When examining the results of the clinical course and prognosis of the work presented here in relation to other studies, some general comments can be made.

In our study, absolute recovery showed less improvement over the clinical course than the percentage of improvement during the 12-month follow-up. An explanation for this could be that the optimal cut-off point is not well described in earlier studies, making it difficult to choose an appropriate cut-off point compared with the percentage of improvement. This idea is supported by other studies.[3,4,6,8,9,11,33,34,51] Patients with a lower baseline score on the characteristics of low back pain also have less potential for improvement than patients with more severe baseline values. When using our definition for absolute recovery, the latter group need to perceive a greater improvement in order to feel that it is indeed relevant.[52] Another challenge for both definitions is the interpretation of the definition. For example, patients close to but on opposite sides of the cut-off for, e.g., a 30% improvement compared with the baseline score, are characterized as being very different rather than being very similar. Another example is the problem with MCIC values: i.e. a patient with a baseline score of 80 points on the QBPDS will more easily achieve a decrease of 30% (around 24 points) on their disability scale at 5-months follow-up, than the progression from 80 points to less than 20 points (cut-off point of absolute recovery). These findings imply that the choice of a low cut-off value for absolute recovery will entail that fewer patients will recover. Also, a 30% improvement is deceptive, because even a decrease from 80 to 56 points on the QBPDS still represents limitations in daily life for the patient. Unfortunately, variations in the choice of cut-off points hamper comparison of the clinical course over time; moreover, it is then unclear how important this particular change is for the individual patient. Knowing that the course of low back pain varies between individuals, with differences in both duration and intensity, mean it is difficult to determine the 'real value' of recovery. It might be more better to define recovery in consultation with the patient's perspective and with the clinicians, and by means of further prospective research whilst also defining and selecting the most suitable outcome(s).

We selected our prognostic factors and outcomes based on current evidence, theory, and clinical expertise. The Multinational Musculoskeletal Inception Cohort Study Statement (MMICS) described some factors which we also found relevant, e.g. lifestyle (e.g., alcohol consumption, smoking), work-related factors (e.g. job satisfaction, social support) and number of sick days.[53] However, to comply with the rule of at least 10 events per variable in the analysis (which avoids incorrect estimation of variables), we had to restrict the total number of potential prognostic factors.[54] However, in the methodologically robust studies presented in this thesis, the baseline factors only account for a (small) proportion of the variance in outcome, ranging from 2.7% to 59%. In future research, it is recommended to

include additional factors[39,44,55,56] (e.g., social factors, lifestyle factors, work-related factors, patient beliefs). Nevertheless, our study demonstrates stability for over 12 months in the key prognostic factors during both the short and long-term follow-up.

Another important aspect is the description of outcome. For example, terminology such as 'back pain intensity' can be used to refer to the sensation of pain in the back; however, this term is also used to describe a disabling health condition in which the patient can experience functional impairment, difficulties in performing tasks, and/or restricted ability to participate in activities such as work.[57] It may be preferable to combine the outcome 'back pain' and 'disability' into one outcome measurement as, e.g., in the Pain Disability Index (PDI)[58], or to identify distinct groups of back pain patients to improve our understanding of the course of back pain; this may then provide a basis for certain prognostic factors or of (sub)classifications for interventions.[14,44,59,60] One example is based on a multi-domain prognostic model, in which each patient's risk for developing persistent back pain is determined and used to match the patient to an appropriate treatment. This STarT Back (Subgroups for Targeted Treatment) approach was developed to allow choice in the investigation and treatment in primary care decision-making.[61-63]

The MMICS' statement recommends 'days of work' for the outcome work.[53] However, we were unable to retrieve this information from our data and therefore used work participation (dividing 'current work hours' by 'former work employment hours' prior to chronic non-specific low back pain) as outcome. This definition has not been used before, because the clinometric values are unknown, thereby making comparison of the results difficult. VAS pain intensity, QBPDS, and GPE are frequently used outcome instruments.[3,4,51,64] In our studies we used the GPE 5-point scale without the option 'completely recovered'. Kamper et al. conclude that the rating of the GPE scale is strongly influenced by the patient's current health status and this may increase with longer transition times into months (recall bias and/or measurement bias).[48] Errors in the interpretation of the measurement (confounding) can also be made by therapists and/or researchers. This type of information raises the question as to whether transition ratings truly reflect change or, rather, only the current state of health.[48] When assessing the GPE, it remains unclear what this measure actually represents for patients with chronic non-specific low back pain. One study reported that the GPE captures a patient's perception of change in various domains that are important for their individual pain experience, i.e. items which may not be captured by other outcome instruments[65] however, this latter study was performed among neck pain patients only.

The identification of factors predictive of a higher impact of chronic non-specific low back pain on quality of life would help to define management Stategies. We used the quality of life questionnaire (SF-36) which has several (sub)scales besides the PCS and MCS. The validity of the scores for several (sub)scales of the SF-36 need to be taken into consideration as they contain many items which are not

practical for clinical use. At baseline, patients who had recently suffered an exacerbation, or had recovered during follow-up, may have had difficulty in rating their status during the period of evaluation and may have been influenced by their perceptions at the time of assessment.[55,66] This might be a reason for the 28% missing data. A simpler and shorter questionnaire might alleviate this problem; for example, instead of using the complicated SF-36, use a VAS assessing 'global quality of life' (which has demonstrated good validity and reliability).[67] On the other hand, this might result in some loss of information. The MMICS teams also recommended to include outcome measures on psychological factors, and diaries to measure utilisation of care and medication consumption, or satisfaction with care.[53] In future prospective cohort studies, the research group needs to (re-) consider baseline factors, outcome factors and which measures to use, since knowledge is lacking on all the complicated areas in which chronic non-specific low back pain is manifested.

In summary, this work has shown that some baseline characteristics are associated with recovery. This provides better insight into chronic non-specific low back pain, which can help researchers and clinicians to be better informed about their patients, the possible clinical course and the patient's potential to recover. The next research steps will involve external validation of our models and a feasibility study, before implementation of our prognostic models is possible in clinical practice.[68,69]

Study limitations

All studies have some limitations that should be addressed; this is also the case for the work presented here.

The question arises as to whether it is wise to conduct a prospective cohort study with a maximum of 12 months follow-up after a 5-month therapy program (2 months SJC and 3 months self-management), knowing that chronic non-specific low back pain has an unknown course and that the duration to recovery may take longer than expected. In our study population the duration of complaints was (on average) 7.7 years. Recent studies report that most patients with back pain appear to follow a particular pain trajectory over a longer time period, and do not have frequently recurring widely fluctuating patterns.[59,60] It is possible that a particular pain trajectory will have certain clinical characteristics and that this might influence which prognostic factor is important and also the eventual result of a rehabilitation program.[59]

The present study collected data at the SJC rehabilitation centre during daily practice. For the baseline data (0-28% missing values) this was relatively successful. The standard electronic patient files provided most of the information on the variables at baseline and up to the 5-month follow-up; additional data were acquired via paper questionnaires.

At the 5 (location SJC) and 12-month (postal questionnaires) follow-up, 11.1% and 45.2% of the patients (n=1,760), respectively, failed to submit the follow-up data. There are various reasons for this loss of data. For example, the SF-36 information (28% missing values at the baseline) was collected both electronically and, separately from the other data, at the start of therapy by a therapist; on some occasions this step was forgotten. Other reasons could be that the Dutch terminology used in the questionnaire was too difficult for the patient, or an incomplete questionnaire was returned. The physician performed the baseline measurements and a therapist carried out the 5-month follow-up measurement. Although both the physician and therapist followed a protocol, some differences may have occurred. At the 5-month follow-up, loss of data was due to several reasons, e.g. abandoning the protocol during the course of conversation with the patient, time management, patient forgot an appointment, and/or there was no check to see whether all data were collected, etc. At the 12-month follow-up, the postal questionnaires were also subject to loss of data., e.g. the patient was on vacation, the envelope was not stamped, the patient had completely recovered from chronic non-specific low back pain or had started another intervention, the SJC's policy of not sending a reminder to the patient, and no electronic collection of the data. Each time that data were collected, this involved information on over 100 variables; this can lead to overload for the patient and may result in lack of participation and/or incomplete questionnaires.

Also, because most of our data are based on self-reported questionnaires, we cannot exclude possible overestimation/underestimation of the patients' complaints. Although the validation and reliability are acceptable (Chapter 3), from the patient's perspective other interests may be involved when answering the questionnaire (e.g. role in the family, social benefits, beliefs and perception about illness).

Missing data and the impact of non-response at baseline and follow-up were analysed by comparing patients' baseline response on individual prognostic factors with those at 5- and 12-months follow-up. There were no reported differences between responders and non-responders on the main outcomes. However, some non-responders may have difficulty in implementing new behaviour and changed cognitions from one setting to another, or in remaining compliant to the therapy. Also, these patients may have already undergone at least some kind of unsuccessful treatment and are, therefore, more cautious regarding the interventions offered and the effect upon themselves. To obtain more insight into this topic, or in the subgroup who do not recover, an option is to use the credibility/expectancy questionnaire (CEO) before the start of intervention and again at the follow-up.[70] For patients who do not recover during the long-term follow-up, a 'refresher prevention session' might be necessary. Also, further research on the effectiveness of the intervention of the SJC protocol may be advisable.

Some general changes can be recommended for health policies regarding how to continue to inform, socially interfere as clinician[31] and motivate the patient to follow the therapy strategy, in order to tackle the problem of persisting/recurrent low back pain after an intensive rehabilitation period.

Comparison of our patients with other study populations has both limitations and challenges. First, our patients were recruited from a rehabilitation centre of tertiary care with a multidisciplinary cognitive behaviour therapy, in contrast with many studies which were conducted in primary care and among the general population.[23,71] There is a possibility of selection bias, e.g. our cohort is not an inception cohort and this may influence the clinical course through the selection of patients. Our patients may have more complex conditions and/or complaints and may be dealing with additional factors that may influence recovery.[22] In many studies low back pain is not clearly defined[72]; we conformed to the (inter)national definitions and selection criteria[73] to ensure as far as possible that our patients are a good reflection of the chronic non-specific low back pain population. Our study did suffer from loss to follow-up, which implies a smaller number of patients for the full analysis. Also, the quality of the data depends on the completeness of registration by the patient, care.g.ivers, administrative staff and/or researchers. The possibility of selection bias and residual confounding cannot be ruled out. It would be better if all data could be collected electronically and with timely reminders.

Prognostic research and methodological issues

Developing useful prognostic models to predict recovery in daily clinical practice is not simple. Chronic non-specific low back pain fluctuates over time and some methodological issues need to be addressed. There are three main types of prognostic study: 1) the prognostic course studies, 2) prognostic (explanatory) factor studies, and 3) outcome prediction (risk group) studies.[74] Our patients were seeking help in tertiary care[75] were recruited, and then we described their clinical course.

We performed the most common type of prognostic research, i.e. investigation, exploration and identification of potential prognostic factors.[69,74] Hayden et al. report that this gives the least conclusive information regarding the independence of the variable as a valid prognostic factor.[74] Through our systematic review (Chapter 3) we concluded that for chronic non-specific low back pain only a few studies have examined our 5 outcome measurements and that the majority of these are of low methodological value, making it necessary to conduct this type of study.[69]

There are different ways to derive prognostic models and also different statistical approaches, all of which can lead to differences in prognostic models.[74,76]

First, when dealing with missing data we decided to use the multiple imputation procedure, as this is assumed to be more valid than simply omitting these patients from the analysis.[10] Another consequence is that it reduces the sample size/power and thus the model's validity.[12,77,78] By performing sensitivity analyses and completed cases analyses (CCA), we validated our models in the population.[79-81] In our studies (Chapters 4-7) this revealed little to no difference in the identified prognostic factors, indicating that these models were relatively stable. Furthermore, in all analyses, the CCA showed slightly higher standard errors (SEs) and coefficients compared with the imputed datasets. This indicates that, as expected, both the power and the precision were increased by use of imputation.[81]

The C-index or area under the curve (AUC) and the explained variance showed a range of 0.65-0.90 and 2.7-59%, respectively (Chapter 4-7). The AUC may give a general estimation of the discriminative ability of a prediction model, but is not directly meaningful for clinical purposes.[74] In low back pain it is not uncommon for prognostic factors to show a significant association with the outcome at group level, but little prognostic value at the individual level; also, there is no evidence for a single factor that substantially affects low back pain prognosis on its own for all individuals.

In our study we chose to split some continuous variables into two or more cate.g.ories during the development of the multivariable logistic regression models. The advantage of this categorisation or dichotomising is that it simplifies the interpretation of the model and the application to clinical practice.[12] We did this for all outcome measurements, i.e. dichotomising the variable into 'no improvement' vs. 'improvement' with either the percentage of improvement and/or the so-called 'optimal' cut-off points, absolute recovery.[4,5,64] This can introduce additional bias in the analysis (e.g., overestimation of the discriminative ability) which carries the risk of a poorer performance model.

Implications for daily practice

For daily practice this thesis provides preliminary evidence for clinicians and patients in tertiary care about the clinical course of back pain and which prognostic factors have most influence in the recovery from chronic non-specific low back pain. The evidence remains preliminary because external validation is required and the impact on daily practice still needs to be examined.[68,69] Nonetheless, we provide evidence that some patients with chronic non-specific low back pain show improvement in the clinical course during the 12-month follow-up and that the following domains help to predict possible recovery during follow-up: patients' characteristics (younger age, female, being married or living with one adult), clinical status (present back pain intensity, disability, higher physical quality of life at baseline), psychological factors (higher score on the mental part of

quality of life at the baseline), and work-related factors (higher work participation at baseline). The domain 'physical examination' was only sporadically applied.

A substantial proportion of the patients in this study experienced repeated episodes or recurrences of low back pain, whereas another proportion reported continuous symptoms over many years.[13,16,19,21] During the 12-month follow-up, some patients recovered from back pain, others sporadically experienced back pain, and others continued to suffer from back pain most of the time.[39,59,60] Non-specific low back pain is not a self-limiting disease in all patients; a large proportion of patients experience persistent low-intensity pain and disability, but are able to return to work[82] this has been confirmed in our studies. Awareness of the impact of low back pain may help physicians and therapists to better inform the patient about their course of chronic non-specific back pain.

Regular use of patient-reported outcome measures (PROMs)[83], which is more common in tertiary care, should be further implemented in Dutch primary and secondary care. This will provide clinicians with more insight into the clinical course and identification of potential subgroups and makes comparison of results with tertiary care possible. For some questionnaires more evidence is required, or a shorter and simpler questionnaire should be developed for daily practice. In addition, for general health care the questionnaire should capture the impact of items related to the patient-clinician relationship and the patient's contribution to their own recovery.[84]

Current treatments regularly use or incorporate techniques drawn from cognitive behavioural therapy. Cognitive behavioural therapy focuses on the beliefs, feelings, and behaviours of pain patients, most often concentrating on the pain experience (e.g. fear avoidance, catastrophising). However, our results show that fear avoidance was not an important variable in our sample of chronic non-specific low back pain patients.[2,85]

Our results suggest that additional attention should be paid to patients' psychological factors, their clinical course of back pain intensity, disability, and their work participation. All these components can also be implemented in primary and secondary (outpatient clinic) care; however, close collaboration with other disciplines/professionals that have the same vision/goals, and are available during the same period, will be difficult to achieve. We are unable to demonstrate the effect of the cognitive behaviour therapy combined with supervised exercises, education and a multi-disciplinary treatment; however, Cochrane reviews have shown a greater improvement on the short term than other forms of treatments.[28,86]

Implications for further research

Clinical course

The research conducted in this thesis concerned the description of the 5 outcome measurements at the 2-, 5- and 12-month follow-up. Further research on the clinical course should include study of the prognosis using more frequent and longer follow-up periods (up to 5-10 years or the life-course).[39,59,60] This will help researchers and clinicians to better understand the patterns of recovery and change over time[74] and to identify different subgroups. Further research is also required to establish which patients should enter the SJC, can receive other interventions within the therapy program, or are in need of more guidance and/or longer follow-up programs. Also, for the MCIC on absolute recovery (cut-off point) more insight is required into the probable course, and information on the expectations and views/experiences of the clinician and patient is also desirable.

Prognostic research

For all 5-outcome measurements, several prognostic models were developed and internally validated. Collaboration with other rehabilitation centres would help to combine focus on the external validation of these results on the 5 outcomes and their feasibility for daily practice.[68,69,77] This investigation needs to take place before implementation into daily practice and into guidelines.[87] Once the prognostic factors for recovery have been identified and validated, more studies are needed to examine whether these prognostic factors influence the recovery rate in patients with chronic non-specific low back pain. Effective models provide more accurate predictions that inform patients and caregivers, support clinical research and allow informed decisions to improve patient outcomes – especially by means of a bio-psycho-social model. Thus, rather than (always) developing new models from scratch, we should consider whether existing models can be improved by recalibration or by adding prognostic factors, such as findings from physical examinations.[69]

Before improving the models, additional research should determine whether the MCIC can be better expressed as a percentage of improvement, or in scale points of absolute recovery (cut-off point), including the patient's and clinician's view on this topic.

Further development and enhanced cooperation with other research groups regarding the existing international standard core set[53] and statistical techniques might also enable better comparison of the results and more appropriate interpretation of the dynamic (clinical) nature of chronic non-specific low back pain between different studies and/or countries. To have a multi-domain prognostic model, where each patient's risk for persistent chronic non-specific low back pain is determined and used to match the patient to the most optimal treatment, would be an important asset.

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SUMMARY

Chapter 1 is an introduction of the topic and aims of this thesis. The overall aim of this thesis was to acquire knowledge about the clinical course and identify clinically important prognostic factors (including internal validation) of patients with chronic non-specific low back pain receiving cognitive behaviour therapy in a tertiary multidisciplinary setting. The outcomes of interest were: back pain intensity, disability, work participation, quality of life and global perceived effect.

In **Chapter 2** we describe a systemic review based on the literature available in PubMed, CINAHL and EMBASE (through March 2010) in order to retrieve prognostic factors for low back pain intensity, disability, return to work, quality of life, and global perceived effect in patients with chronic non-specific low back pain on short-term (≤ 6 months) and long-term (> 6 months) follow-up. After applying the inclusion/exclusion criteria 14 studies were included, most of them reporting on the outcomes of low back pain intensity and disability. The included studies used different definitions for the outcomes and prognostic factors. Most of the studies (71%) were considered to have a high risk of research bias. When considering the outcomes of low back pain intensity and disability, the results showed no associations with age and sex on short-term follow-up, and with smoking on long-term follow-up. Conflicting evidence was found for 'fear of movement' and the outcomes of low back pain intensity and disability on short-term follow-up. On long-term follow-up, baseline low back pain intensity and 'fear of movement' had no association with the outcome disability. On long-term follow-up, conflicting evidence was found for an association between the factors age, sex, and physical job demands, and the outcomes of low back pain intensity and disability. On long-term follow-up, conflicting evidence was found for an association between the factors age, sex, activities of daily living and mobility, and the outcome return to work. At baseline, there was limited evidence for a positive influence of lower pain intensity and physical job demands on return to work. No high-quality studies were found for the outcomes quality of life and global perceived effect.

Chapter 3 describes the design and methods of the prospective cohort study. We assessed the baseline characteristics of patients with chronic non-specific low back pain and described the methods used to investigate the clinical course and to identify potential prognostic factors (including internal validation) in a 12-month follow-up study. All participating patients with chronic non-specific low back pain (n=1,760) were recruited between January 2003 and December 2008 at the Spine & Joint Centre rehabilitation centre (mean age 40.1 years, SD 10.6; 73%

female) and were evaluated by means of (postal) questionnaires and physical examinations at baseline, at 2-months follow-up (after the 2-months therapy program), and again at 5 and 12-months follow-up. At the rehabilitation centre, the multidisciplinary behaviour therapy protocol used a bio-psychosocial approach to stimulate patients to adopt adequate (movement) behaviour aimed at physical and functional recovery. The program consists of 16 sessions of 3 hours each over an 8-week period (in total 48 hours), followed by a 3-month self-management program (e.g. exercises twice a week). The primary outcomes were back pain intensity, disability, work participation, quality of life, and patient's global perceived effect.

Each model had the same 23 potential prognostic factors. The factors for the domain 'patient' characteristics' were: age, gender, educational level (less than high school vs. high school/university), body mass index (BMI ≤ 24.9, 25-29.9, ≥ 30 kg/m^2) and marital status/living with one adult (no/yes). For clinical status the following factors were included: duration of back pain in years, cause of back pain (accident movement; after physical load; during pregnancy or after delivery; unknown; surgery pelvis/back or HNP), previous rehabilitation treatment (none vs. one or more previous rehabilitation treatments), comorbidity (none vs. having one or more co-morbidities), present pain intensity (Visual Analogue Scale (VAS) 0-100 mm; with higher scores indicating more pain), course of pain in the previous 3 months (stable; increased; decreased), degree of present fatigue (VAS 0-100 mm; with higher scores indicating more fatigue) and the Quebec Back Pain Disability Scale (QBPDS; 0-100; with higher scores indicating more disability). Psychological factors were: the Dutch version of the Tampa Scale for Kinesiophobia (TSK-DV, 17-68; with a higher score indicating more pain-related fear), SF-36 MCS and PCS at baseline (0-100; with higher scores indicating better quality of life), and the Symptom Checklist 90 (SCL-90; item 9; psychoneurosis). Domain work-related factors consisted of two prognostic factors, work participation (0-100%; by dividing 'current work hours' by 'former work employment hours' prior to chronic non-specific low back pain) and sickness benefit (none vs. receiving different types of government welfare benefits). Finally, the domain physical examination consisted of the B200 Isostation (strength of back extension in Newton) and the duration of walking, sitting, standing (0-15, 16-30, 31-60, > 61 min) during daily activities.

In our study, every outcome for recovery was operationalised according to two definitions: 1) 30% improvement during follow-up compared to the baseline score for the outcome back pain intensity, disability and work participation and a 10% improvement in the score on the SF-36 PCS and MCS, and 2) 'absolute recovery' was defined as a VAS score of ≤ 10 mm, a QBPDS score of ≤ 20 points, work participation working (0-100%) ≥ 90% at follow-up, and global perceived effect on a 5-point scale (GPE) dichotomized into 'clinically improved' vs. 'clinically not improved'.

Multivariable logistic regression analysis included the 23 baseline characteristics with imputed datasets of 5 models and a p-value of 0.157. A sensitivity analysis was performed; the selection of variables was repeated in imputed datasets of 5 and 40 models with p-values of 0.05 and/or 0.157, respectively. We also compared

the results with complete-case analysis, i.e. all patients with missing data were excluded from the analyses. Furthermore, every outcome was also changed regarding the percentage improvement and/or absolute recovery score (cut-off point) during the sensitivity analysis.

The results of our prospective cohort study are described in Chapters 4 to 7.
In **Chapter 4** we assessed the clinical course and potential prognostic factors (including internal validation of the models) for recovery defined with the outcome back pain intensity at 2, 5 and 12-months follow-up. Patient-reported back pain decreased from 55.5 (SD 23.0) at baseline to 37.0 (SD 23.8), 35.3 (SD 26.1) and 32.3 (SD 26.9) at 2, 5 and 12-months follow-up, respectively. At 12 months, 61% of the patients experienced a 30% improvement and 29% of the patients an absolute recovery (VAS ≤ 10 mm) with regard to back pain intensity.

At 5-months follow-up, a 30% improvement resulted in a final model (AUC=0.66) which included 9 prognostic factors, together explaining 11% of the variation in outcome: younger age, female gender, a baseline BMI > 25 kg/m^2, no previous rehabilitation treatment, higher baseline level of back pain intensity, no psycho logical/physical dysfunction, higher baseline scores on the SF-36 (PCS and MCS), and higher work participation at baseline. At 12-months follow-up the following factors were related to a 30% improvement: younger age, female gender, being married/ living with one adult, higher level of education, no comorbidity, higher back pain intensity, higher strength at the extension direction, no fear of movement, and higher scores on the PCS (SF-36), with a 10% explained variance and an AUC of 0.65.

At 5 and 12-months follow-up, for absolute recovery the explained variance was 11% and 18%, respectively, with an AUC of 0.69 and 0.73, respectively. At 5 and 12 months the factors younger age, less back pain intensity at baseline and higher scores on the SF-36 were prognostic factors for back pain intensity. Also added to the 5-month follow-up were the factors: no psychological/physical dysfunction, and more work participation at baseline. At baseline, a BMI ≥ 30 kg/m^2, no comorbidity, higher disability score and having stable or more back pain intensity due to chronic non-specific low back pain in the previous 3 months were added to the 12-month follow-up. For every prognostic model, the internal validation showed identical results in experienced variance and AUC as in the developed prognostic models. The sensitivity analyses (e.g. ≤ 20 mm VAS) also showed similar results.

Chapter 5 reports on the clinical course of and prognostic factors (including internal validation) for recovery defined with the outcome low-back-pain-specific disability in patients with chronic non-specific low back pain at 2, 5 and 12-months follow-up. The results show that the mean disability scores on the QBPDS decreased from 51.7 (SD 15.6) at baseline to 31.7 (SD 15.2), 31.1 (SD 18.2), and 29.1 (SD 20.0) at 2, 5 and 12 months, respectively. At 12-months follow-up, 63% of the patients reported a 30% improvement in disability.

Absolute recovery (QBPDS ≤ 20) increased to 24%, 31% and 38% at 2, 5 and 12 months, respectively.

The following prognostic factors were identified for a 30% improvement on disability at 5 and 12 months: younger age, being married or living with one adult, higher baseline score on disability, higher scores on the SF-36, and no previous rehabilitation program. In addition, at 5 months, having more work at baseline, a decreased course of pain in the previous 3 months before the start of therapy, and a short duration of back complaints, were additional predictors (explained variance 12.8% and an AUC of 0.68). At 12 months the additional factors in the model were: having no comorbidity, higher educational level, and less back pain at baseline (explained variance 10.7% and an AUC of 0.66).

For the outcome absolute recovery (≤ 20 QBPDS) younger age, shorter duration of back pain complaints, lower baseline score on disability, and higher score on the SF-36 were similar for 5 and 12-months follow-up. The 5-month follow-up showed an explained variance of 2.7% and an AUC of 0.66 with the addition of the factor no psychological/physical dysfunction. For the 12-month follow-up, having no comorbidity at baseline, less back pain intensity, ≤ 60 min walking duration, and strength in the trunk, were added to the model, with an explained variance of 10.7% and an AUC of 0.66.

With regard to internal validation of the models and the sensitivity analysis, the values were similar. The sensitivity analysis was performed using the QBPDS cut-off values of ≤ 10 and ≤ 39 points and showed similar results.

Chapter 6 describes the clinical course and recovery as defined with the outcome work participation (0-100%) in patients with chronic non-specific low back pain. For these analyses we included 1,608 patients, i.e. those reporting to have a paid work contract at baseline. The outcome was work participation: this was defined by dividing 'current work hours' by 'prior contract work hours'. Patients reported an increase in work participation from 38% (SD 43.1) at baseline to 73% (SD 44.9) and 82% (SD 52.9) at 5 and 12 months, respectively. Regarding the 30% improvement in work participation, this was 30.3% at 5-months and 60.5% at 12-months follow-up. At baseline, 25.4% of the patients worked ≥ 90% when weighted against the absolute value of recovery; this increased from baseline to 43.2% and 52% at 5 and 12 months, respectively. At 5 months, for the outcome 30% improvement in work participation, the following prognostic factors were found: less back pain intensity at baseline, low percentage of work participation, duration of standing (31-60 min) and the cause (accident or wrong movement), with an explained variance of 59% and an AUC of 0.89. At 12-months follow-up the multivariate regression model (AUC=0.90) consisted of 4 prognostic factors explaining 60% of the variation: younger age, higher education, low percentage of work participation at baseline, and a higher MCS (SF-36) at baseline. Prognostic factors for 'absolute recovery' (≥ 90% work participation) at 5 months were being married or living with one adult, female gender,

higher disability score, higher score on the PCS SF-36, previous rehabilitation, not receiving sickness benefits, and higher work participation at baseline. Higher work participation at baseline and female gender were also prognostic factors for 'absolute recovery' at 12-months follow-up. At 5-months follow-up the explained variance was 30% and the AUC 0.78 whereas it was 17% and 0.70, respectively, at 12-months follow-up. The internal validation of the models and the sensitivity (cut-off values of 80% working and 100% working) showed similar results.

In **Chapter 7** we investigated the clinical course of and identified prognostic factors for the outcomes quality of life and global perceived effect in patients with chronic non-specific low back pain at 5 and 12-months follow-up.

Patients reported an increase of the MCS and PCS (SF-36) from on average 46.6 (SD 10.3) at baseline to 49.2 (SD 9.4) at 5-months follow-up for the MCS compared to 31.9 (SD 7.1) at baseline to 40.7 (SD 8.2) for the PCS. A 10% improvement on the MCS and PCS was reported by 39.6% and 76.6% of the patients, respectively, at 2 months, and by 20.6% and 76.3% of the patients, respectively, at 5-months follow-up. At 2 months 45.1% reported a clinical improvement using the GPE scale; this improvement increased to 53.0% and 60.3% at the 5 and 12-months follow-up, respectively.

Baseline variables showing an association with a 10% improvement on the PCS (SF-36) at 5-months follow-up were: younger age, BMI of ≥ 30 kg/m^2, lower score on the PCS (SF-36), higher score on the MCS (SF-36), psychological/physical dysfunction, receiving sickness benefit, having more work at baseline, and duration of walking of 16-30 min. The following baseline variables were associated with a 10% improvement of the MCS (SF-36) at 5-months follow-up: female gender, higher score on the PCS (SF-36), lower score on the MCS (SF-36) and no psychological/physical dysfunction (SCL-90, item 9). The AUCs were 0.69 and 0.88, respectively, and the explained variance was 11% for the PCS and 44% for the MCS SF-36. Younger age, being married or living with one adult, shorter duration of back pain complaints at baseline, lower back pain intensity, and working more often at baseline were associated with a clinical improvement on the GPE at 5 and 12-months follow-up. At 5 months the explained variance was 11% and the AUC was 0.66. At 5 months additional factors were included such as decrease of back pain intensity in the previous 3 months before baseline, higher disability, no fear of movement, higher score on the MCS and the PCS SF-36, receiving sickness benefit, and strength. At 12-months follow-up the factors being female and duration of walking (16-30 min) were added to the model with an explained variance of 9% and an AUC 0.65 for the total prognostic model. The internal validation and sensitivity analysis (30% improvement on the MCS and PCS) showed similar results.

Chapter 8 addresses the main findings and limitations of the studies described in this thesis, discusses implications for daily practice, and makes some recommendations for further research.

SAMENVATTING

Hoofdstuk 1 vormt een inleiding op het onderwerp en de doelstellingen van dit proefschrift. De algemene doelstelling van dit proefschrift was het verkrijgen van kennis van het klinische beloop en de identificatie van potentiële prognostische factoren (inclusief interne validatie) voor herstel bij patiënten met chronische aspecifieke lage rugpijn, die een cognitieve gedragstherapie in een tertiaire multidisciplinaire setting hebben gevolgd. Hierbij stonden de volgende patiëntgebonden uitkomstmaten centraal: rugpijnintensiteit, beperkingen in activiteiten door de rugpijn, werkparticipatie, kwaliteit van leven en ervaren herstel.

In **hoofdstuk 2** is er systematisch in de literatuur gezocht, die beschikbaar was in PubMed, CINAHL en EMBASE (tot maart 2010), ter verkrijging van informatie over prognostische factoren bij patiënten met chronische aspecifieke lage rugpijn. Identificatie van prognostische factoren heeft plaatsgevonden voor de uitkomstmaten rugpijnintensiteit, beperkingen in activiteiten, werkparticipatie, kwaliteit van leven en ervaren herstel in de follow-up op korte termijn (≤ 6 maanden) of op langere termijn (> 6 maanden). Na toepassing van de insluit- en uitsluitcriteria zijn er 14 studies geïncludeerd. De meeste studies betroffen onderzoek naar de uitkomstmaten rugpijnintensiteit en beperkingen in activiteiten.
Het onderling vergelijken van de studies was moeilijk, omdat de uitkomstmaten op verschillende manieren gedefinieerd en gemeten waren, met daarnaast een diversiteit aan prognostische factoren. Ook waren de meeste studies van mindere methodologische kwaliteit.

In de korte termijn follow-up zijn geen associaties gerapporteerd van de uitkomstmaten rugpijnintensiteit en beperkingen in activiteiten met de factoren leeftijd en geslacht, en in de langere termijn follow-up niet met de factor roken. In de korte termijn follow-up is tegenstrijdig bewijs gevonden voor een relatie tussen de uitkomstmaten rugpijnintensiteit en beperkingen in activiteiten en de factor angst om te bewegen. Op langere termijn vertoonden de intensiteit van de rugpijn op baseline en de factor angst om te bewegen geen associatie met de uitkomstmaat beperkingen in activiteiten. Voor de langere termijn is tegenstrijdig bewijs gevonden voor een relatie tussen de uitkomstmaten rugpijnintensiteit en beperkingen in activiteiten en de factoren leeftijd, geslacht en fysieke componenten. Voor de langere termijn is ook tegenstrijdig bewijs gevonden voor een relatie tussen de uitkomstmaat werkparticipatie en de factoren leeftijd, geslacht, dagelijkse activiteiten in het leven en mobiliteit.

Er is weinig bewijs gevonden voor een positieve invloed van een lage rugpijnintensiteit en fysieke componenten binnen het werk op de uitkomstmaat werkparticipatie. Er zijn geen studies gevonden met hoge methodologische kwaliteit voor de uitkomstmaat kwaliteit van leven en door de patiënten ervaren herstel.

De methode van het uitgevoerde prospectieve cohort onderzoek is beschreven in **hoofdstuk 3**. Ook zijn de baselinegegevens van de patiënten met chronische aspecifieke lage rugpijn gepresenteerd en de methoden voor het bepalen van het klinisch beloop en de identificatie van potentiële prognostische factoren (inclusief interne validatie) gedurende een follow-up van 12 maanden. Alle deelnemende patiënten zijn geworven tussen januari 2003 en december 2008 bij het Spine and Joint Centre (gemiddelde leeftijd 40,1 jaar, SD 10,6; 73% vrouw). Patiënten hebben vragenlijsten ingevuld en zijn lichamelijk onderzocht aan het begin van het onderzoek en 2, 5 en 12 maanden na de start van de therapie. De therapie binnen het revalidatiecentrum heeft een bio-psychosociale benadering, waarbij patiënten worden gestimuleerd om op adequate wijze te bewegen, gericht op fysiek en functioneel herstel. Het programma bestaat uit 16 bijeenkomsten van elk drie uur over een periode van acht weken (in totaal 48 uur). Patiënten volgen daarna drie maanden lang een ''self-management''-programma buiten het revalidatiecentrum. De primaire uitkomstmaten waren rugpijnintensiteit, beperkingen in activiteiten, werkparticipatie, kwaliteit van leven en ervaren herstel.

Er zijn 23 potentiële prognostische factoren onderzocht voor elke uitkomstmaat. De factoren voor het domein patiëntenkenmerken waren: leeftijd, geslacht, opleidingsniveau (minder dan de middelbare school versus middelbare school/universiteit), body mass index (BMI: ≤ 24,9, 25–29,9, ≥ 30 kg/m^2) en getrouwd/samenwonend met een volwassene (ja/nee). De factoren voor het domein klinische kenmerken, allemaal gemeten op baseline, waren: duur van de rugpijn in jaren, oorzaak van de rugpijn (ongeval/na lichamelijke belasting/tijdens de zwangerschap of na de bevalling/onbekend/chirurgie aan het bekken, rug of HNP), eerdere revalidatiebehandeling (geen/een of meerdere revalidatiebehandelingen), comorbiditeit (geen/een of meerdere comorbiditeiten), rugpijnintensiteit op baseline (Visuele Analoge Schaal, VAS; 0–100 mm; een hogere score staat voor meer rugpijn), beloop van de pijn in de voorafgaande drie maanden (stabiel/toenemend/afnemend), vermoeidheid (VAS; 0–100 mm; een hogere score staat voor meer vermoeidheid) en beperkingen (Quebec Back Pain Disability Scale, QBPDS; 0–100; een hogere score staat voor meer beperkingen). De psychologische factoren gemeten op baseline waren: bewegingsangst (Tampa Schaal voor Kinesiofobie, TSK-DV, 17–68; een hogere score staat voor meer pijngerelateerde angst om te bewegen), SF-36 mentale (MCS) en fysieke (PCS) componenten bij baseline (0–100; een hogere score staat voor een betere kwaliteit van leven) en geestelijke en lichamelijke klachten (Symptom Checklist 90, SCL-90, item 9; psychoneurose).

De werkgerelateerde factoren bestonden uit: werkparticipatie (0–100%, door het delen van 'huidige werkuren' door 'voormalige werkuren voorafgaand aan de chronische aspecifieke lage rugpijn') en arbeidsongeschiktheid (wel/niet). Ten slotte bestonden de factoren uit het domein lichamelijk onderzoek uit: spierkracht van de rug (B200 Isostation, in Newton) en duur van het lopen, zitten en staan (0–15, 16–30, 31–60, > 61 minuten) tijdens dagelijkse activiteiten.

In deze studie is herstel voor elke uitkomstmaat geoperationaliseerd in twee definities:

1) Herstel is gedefinieerd als 30% verbetering op het meetmoment in de follow-up in vergelijking met de baselinescore, voor de uitkomstmaten rugpijnintensiteit, beperkingen in activiteiten en werkparticipatie en als 10% verbetering voor de uitkomsten SF-36 PCS en MCS;
2) Absoluut herstel is gedefinieerd als een VAS-score van ≤ 10 mm, een QBPDS-score van ≤ 20 punten en een werkparticipatie van ≥ 90% en door de patiënt ervaren herstel is gedichotomiseerd in 'klinisch verbeterd' versus 'klinisch niet verbeterd'.

Er is een multivariabele logistische regressieanalyse (5 datasets en een p-waarde van 0,157) uitgevoerd met de 23 baseline factoren voor elk van de vijf uitkomstmaten. Een sensitiviteitsanalyse is uitgevoerd, waarbij de selectie van factoren met 5 en 40 geïmputeerde datasets en met een p-waarde van 0,05 en/of 0,157 is gemaakt. We hebben een completed-case-analyse (CCA) uitgevoerd, dat wil zeggen dat alle patiënten van wie gegevens ontbraken, van de analyses waren uitgesloten. Ook zijn voor elke uitkomstmaat het percentage van de verbetering en/of de score van het absolute herstel (afkappunt) aangepast, om de invloed hiervan nader te onderzoeken.

De resultaten van het prospectieve cohort onderzoek zijn beschreven in de hoofdstukken 4 tot en met 7.

In **hoofdstuk 4** is het klinische beloop beschreven en de identificatie van prognostische factoren (met de interne validatie van de modellen) die gerelateerd zijn aan de uitkomstmaat rugpijnintensiteit in de follow-up na 2, 5 en 12 maanden. De rugpijnintensiteit daalde van 55,5 mm (standaarddeviatie, SD, was 23,0) op baseline tot respectievelijk 37,0 mm (SD 23,8), 35,3 mm (SD 26,1) en 32,3 mm (SD 26,9) op 2, 5 en 12 maanden follow-up. Op 12 maanden follow-up gaf 61% van de patiënten 30% verbetering aan en 29% van de patiënten gaf absoluut herstel (VAS ≤ 10 mm) aan met betrekking tot de uitkomstmaat rugpijnintensiteit.

Het model met de uitkomstmaat 30% verbetering op 5 maanden follow-up resulteerde in 9 prognostische factoren (AUC 0,66), met een verklarende variantie van 11%. De factoren waren: jongere leeftijd, vrouwelijk geslacht, BMI van > 25 kg/m^2, geen eerdere revalidatie behandeling, hogere intensiteit van rugpijn, geen psychische fysieke dysfunctie, hogere scores op de SF-36 (PCS en MCS) en hogere werkparticipatie.

In de follow-up na 12 maanden zijn de volgende factoren betreffende 30% verbetering gevonden: jongere leeftijd, vrouwelijk geslacht, getrouwd/samenwonend met een volwassene, hoger opleidingsniveau, geen comorbiditeit, hoge intensiteit van rugpijn, meer spierkracht richting extensie, geen angst voor beweging en hogere score op de PCS (SF-36) met een verklarende variantie van 10% en AUC van 0,65.

Voor absoluut herstel was de verklarende variantie op 5 en 12 maanden follow-up respectievelijk 11% en 18%, met een AUC van 0,69 en 0,73. Op 5 en 12 maanden follow-up waren jongere leeftijd, lagere intensiteit van de rugpijn en hogere score op de SF-36 de gemeenschappelijke prognostische factoren met betrekking tot de uitkomstmaat rugpijnintensiteit. Ook overgebleven in het eindmodel in de follow-up na 5 maanden waren de factoren: geen psychische of fysieke dysfunctie en hogere werkparticipatie. Toegevoegd aan de follow-up na 12 maanden zijn de factoren: een BMI van ≥ 30 kg/m^2, geen comorbiditeit, meer beperkingen door rugpijn en een stabiele of toenemende rugpijn als gevolg van chronische aspecifieke lage rugpijn in de voorgaande drie maanden. De interne validatie toonde in alle prognostische modellen dezelfde resultaten voor de verklarende variantie en de AUC als in de aangereikte prognostische modellen. Ook de sensitiviteitsanalyse (bijv. ≤ 20 mm VAS) toonde vergelijkbare resultaten.

In **hoofdstuk 5** zijn beschreven het klinisch beloop en de prognostische factoren (inclusief interne validatie) voor de uitkomstmaat beperkingen in activiteiten door rugpijn bij patiënten met chronische aspecifieke lage rugpijn in de follow-up na 2, 5 en 12 maanden. De resultaten toonden aan dat de gemiddelde score op de QBPDS afnam van 51,7 (SD 15,6) op baseline tot respectievelijk 31,7 (SD 15,2), 31,1 (SD 18,2) en 29,1 (SD 20,0) op 2, 5 en 12 maanden. Dertig procent verbetering op de QBPDS-score is gerapporteerd bij 63% van de patiënten na 12 maanden follow-up. Het absolute herstel (QBPDS ≤ 20 punten) nam toe van 24% op 2 maanden follow-up, naar respectievelijk 31% en 38% in de follow-up na 5 en 12 maanden.

De prognostische factoren geïdentificeerd voor 30% verbetering op 5 en 12 maanden follow-up waren: jongere leeftijd, getrouwd/samenwonend met een volwassene, hoge QBPDS-score, hogere score op de SF-36 (PCS en MCS) en geen eerdere revalidatie behandeling. Hierbij waren toegevoegd in het model, op 5 maanden follow-up: hogere werkparticipatie, afname van de pijn in het beloop van drie maanden voor de start van de therapie en kortere duur van lage rug klachten; dit waren positieve voorspellers (verklarende variantie 12,8% en AUC 0,68). Op 12 maanden follow-up waren de aanvullende factoren in het model: geen comorbiditeit, hogere opleiding en lagere rugpijnintensiteit (verklarende variantie 10,7% en AUC 0,66).

Voor de uitkomstmaat absoluut herstel (QBPDS ≤ 20 punten) waren jongere leeftijd, kortere duur van de rugpijn, lagere QBPDS-score en hogere score op de SF-36 (PCS en MCS) opgenomen in het model op 5 en 12 maanden follow-up. Het model op 5 maanden follow-up had een verklarende variantie van 2,7% en een AUC

van 0,66 met de toevoeging van de factor 'geen psychische/lichamelijke dysfunctie'. Op 12 maanden follow-up zijn in de analyse de factoren van geen comorbiditeit, lagere rugpijnintensiteit, duur van wandelen ≤ 60 minuten en spierkracht in de romp toegevoegd aan het model, met een verklarende variantie van 10,7% en een AUC van 0,66.

Voor de interne validatie van de modellen en de sensitiviteitsanalyse (o.a. QBPDS-scores van ≤ 10 en ≤ 39) waren de resultaten ongeveer gelijk.

In **hoofdstuk 6** is het klinisch beloop beschreven en de identificatie van prognostische factoren voor het herstel aangaande werkparticipatie van patiënten met chronische aspecifieke lage rugpijn. In deze studie zijn 1.608 van de 1.760 patiënten geïncludeerd; dit waren de patiënten die – als extra inclusiecriterium op baseline – een arbeidscontract hadden. De uitkomstmaat werkparticipatie is bepaald door het delen van 'het huidige aantal werkuren' door 'het voormalige aantal werkuren, voorafgaand aan de chronische aspecifieke lage rugpijn'.

Patiënten rapporteerden een stijging van de werkparticipatie van gemiddeld 38,3% (SD 43,1) op baseline tot 82% (SD 52,9) na 5 en 12 maanden follow-up. Op 5 maanden follow-up rapporteerde 30,3% van de patiënten 30% verbetering op de score werkparticipatie en op 12 maanden follow-up 60,5% van de patiënten. Op baseline werkte 25,4% van de patiënten voor 90% of meer (absoluut herstel); dit aantal nam toe van baseline naar respectievelijk 43,2% tot 52,0% op 5 en 12 maanden follow-up.

Baseline-factoren die voorspellend zijn voor de uitkomst 30% verbetering in werkparticipatie op 5 maanden follow-up waren: minder rugpijnintensiteit, lagere werkparticipatie, duur van kunnen staan (31–60 minuten) en oorzaak van het ontstaan van de klacht (ongeval of verkeerde beweging), met een verklarende variantie van 59% en een AUC van 0,89. In de follow-up na 12 maanden liet het multivariabele regressiemodel (AUC 0,90) 4 prognostische factoren zien met een verklarende variantie van 60%: jongere leeftijd, hoger opleidingsniveau, lagere werkparticipatie en hogere score op de mentale component (MCS) van de SF-36 op baseline. Prognostische factoren voor absoluut herstel (≥ 90% werkparticipatie) op 5 maanden follow-up waren: getrouwd/samenwonen met een volwassene, vrouwelijk geslacht, een hoge QBPDS-score, een hoge score op de fysieke component schaal (PCS) van kwaliteit van leven (SF-36), eerder hebben gevolgd van een revalidatietraject, geen ziektewetuitkeringen en hogere werkparticipatie op baseline. Hogere werkparticipatie en vrouwelijk geslacht waren ook prognostische factoren voor absoluut herstel op 12 maanden follow-up. Het model voor absoluut herstel op 5 maanden follow-up had een verklarende variantie van 30% en een AUC van 0,78 tegen 17% en 0,70 op 12 maanden follow-up. De interne validatie van de modellen en de sensitiviteitsanalyse (cut-off waarden van 80% werkend en 100% werkend) rapporteerden vergelijkbare resultaten.

In **hoofdstuk 7** is het klinisch beloop beschreven en de identificatie van de prognostische factoren voor ''kwaliteit van leven'' en ''door de patiënt ervaren herstel'' (Global Perceived Effect, GPE) in de follow-up na 5 en 12 maanden bij patiënten (n = 1760) die behandeld waren voor chronische aspecifieke lage rugpijn.

Kwaliteit van leven is gemeten met de Short Form 36-items Health Survey (SF-36). Patiënten rapporteerden een stijging van de MCS en PCS (SF-36) van gemiddeld 46,6 (SD 10,3) op baseline tot 49,2 (SD 9,4) op 5 maanden follow-up op de MCS in vergelijking met 31,9 (SD 7,1) op baseline tot 40,7 (SD 8,2) op de PCS. Tien procent verbetering van de MCS en PCS werd gerapporteerd door 39,6% en 76,6% van de patiënten op 2 maanden follow-up en door 20,6% en 76,3% van de patiënten op 5 maanden follow-up. Op 2 maanden follow-up rapporteerde 45,1% van de patiënten een klinische verbetering op de GPE-schaal en dit nam toe tot respectievelijk 53,0% en 60,3% op 5 en 12 maanden follow-up.

Baseline variabelen die 10% verbetering op de uitkomstmaat PCS (SF-36) op 5 maanden follow-up voorspelden, waren: jongere leeftijd, BMI van ≥ 30 kg/m^2, lagere score op de PCS (SF-36), hogere score op de MCS (SF-36), psychische/lichamelijke dysfunctie, ontvangen van een ziektewetuitkering, hogere werkparticipatie en duur van het wandelen tussen de 16–30 minuten. De volgende baseline variabelen werden geassocieerd met 10% verbetering op de MCS (SF-36) in de follow-up na 5 maanden: vrouwelijk geslacht, hogere score op de PCS (SF-36), lagere score op de MCS (SF-36) en geen psychische/fysieke dysfunctie. De AUC was respectievelijk 0,69 en 0,88 met een verklarende variantie van 11% voor de PCS en 44% voor de MCS van de SF-36. De factoren jongere leeftijd, getrouwd/samenlevend met een volwassene, op baseline kortere duur van de rugpijn, lagere rugpijnintensiteit en hogere werkparticipatie werden geassocieerd met 30% verbetering op de GPE-schaal op 5 en 12 maanden follow-up. De verklarende variantie was 11% en de AUC 0,66 bij 5 maanden follow-up. Aanvullende factoren op 5 maanden follow-up waren vermindering van rugpijn in de voorgaande drie maanden voor baseline, meer beperkingen, geen angst om te bewegen, hogere score op de MCS en PCS SF-36, ontvangen van een ziektewetuitkering en spierkracht. Vrouwelijk geslacht en duur van lopen (16-30 minuten) waren aanvullende factoren in de follow-up na 12 maanden, met een verklarende variantie van 9,0% en een AUC van 0,65. De interne validatie en sensitiviteitsanalyse (30% verbetering op de MCS en PCS) vertoonden resultaten die vergelijkbaar waren met eerdere bevindingen.

Hoofdstuk 8 gaat in op de belangrijkste bevindingen en beperkingen van de studies in dit proefschrift, beschrijft de belangrijkste implicaties voor de dagelijkse praktijk en geeft aanbevelingen voor toekomstig wetenschappelijk onderzoek.

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Hogeschool Rotterdam

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Erasmus MC, afdeling huisartsgeneeskunde

De totstandkoming van dit proefschrift heeft niet kunnen plaatsvinden zonder de bereidheid van medewerking, inzet en betrokkenheid van promotor prof. dr. Bart Koes, co-promoter dr. Pim Luijsterburg en co-promoter dr. Annelies Pool-Goudzwaard.
Pim, met jou als co-promoter heb ik het niet beter kunnen treffen. Jouw focus, prettige overlegstructuur (via de mail altijd een reactie!), je opmerkingen in alle artikelen waarmee ik verder kon, hebben veel bijgedragen aan dit schriftelijk eindproduct.
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Spine & Joint Centre

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Dr. Jan-Paul van Wingerden, directeur en drs. Inge Ronchetti, functie onderzoeker bij het revalidatie centrum zijn mede co-auteurs bij bepaalde studies.
Jan-Paul, jij gunt het dat iemand zich kan ontwikkelen en kansen kan krijgen om het dan ook vorm te geven. Dit doe je voor mij al vanaf mijn studietijd fysiotherapie,

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CURRICULUM VITAE

Karin Verkerk is op 27 november 1974 geboren in Schiedam. Zij behaalde in 1996 haar diploma Fysiotherapie aan de Hogeschool Rotterdam. In 2001 het diploma Gezondheidswetenschappen, richting Bewegingswetenschappen aan de Universiteit Maastricht. Daarop volgde de registratie tot Epidemioloog A in 2001. Op zoek naar een nieuwe uitdaging heeft zij in 2004 het diploma Gezondheidswetenschappen, richting Beleid en Beheer behaald aan de Universiteit van Maastricht.
Vanaf 1997 is zij werkzaam voor de Hogeschool Rotterdam op de opleiding fysiotherapie en naast het reguliere onderwijs verzorgt zij de minor wetenschap en gezondheidszorg en stimuleert de verdere wetenschappelijk onderbouwing van het fysiotherapeutisch handelen. Hiernaast werkt ze ook bij het Spine & Joint Centre (1996-heden), Fysiodocwerk (2001-heden) en aan de Masteropleiding Musculoskeletale Therapie aan de SOMT (2005-heden).
Van 2008-2013 verrichte zij een promotie onderzoek naar het klinische beloop en de prognostische factoren voor herstel bij patiënten met chronische aspecifieke lage rugpijn die een multidisciplinaire behandeling hebben gevolgd bij het Spine & Joint Centre in samenwerking met de afdeling huisartsgeneeskunde van het Erasmus Medisch Centrum te Rotterdam. Haar onderzoek werkzaamheden komen voort uit een promotie voucher, van 2 dagen per week, vanuit de Hogeschool Rotterdam.
Karin is getrouwd met Alexander Peter Both en kregen in 2013 een dochter Sofie.

PhD PORTFOLIO

Summary of PhD training and teaching

Name PhD student:	Karin Verkerk
Erasmus MC Department:	Department of General Practice
University Rotterdam of Applied Sciences:	Department of Health Care
PhD period:	1 September 2008-1 September 2013
Promotor:	Prof. Dr. B.W. Koes
Supervisor:	Dr. P.A.J. Luijsterburg
	Dr. A.L. Pool-Goudzwaard

Conferences

International Primary Care Musculoskeletal Research congress (PRIMUS) - Poster presentation, Rotterdam, 2010	16 hours
International Forum on Low-Back Pain Research in Primary Care - Poster presentation and short oral presentation, Odense, 2012	16 hours
8th interdisciplinary World Congress on Low Back Pain and Pelvic Pain - Poster presentation and short oral presentation, Dubai, 2013	16 hours

Teaching activities

Senior lecturer at the Department of Health Care, Rotterdam University of Applied Sciences, 2008-2013	1 day a week
Lecturer at the Masteropleiding Musculoskeletale Therapie at the SOMT, 2008-2013	1 day a week
Lecturer at the Department of Neuroscience, Erasmus MC, University Medical Center, 2008-2013	120 hours a year
Lecturer of the seminar Low Back Pain and Pelvic Girdle Pain, ''Het Nederlands paramedisch instituut (NPi)'', 2008-2013	32 hours a year

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Karin Verkerk

Chronic Non-Specific Low Back Pain

Chronic non-specific low back pain is assumed to be a multi-factorial affliction, implying that a number of different risk factors contribute to its development and persistence. After onset, prognostic factors can potentially predict the future course. Risk factors for the development of chronic pain (i.e. transition from acute to chronic pain) are well documented in the literature. However, when pain becomes persistent, less knowledge is available on the risk factors for future outcome. Increased knowledge on the prognostic factors for chronic complaints will allow to better inform and advise patients, by supporting clinical decisions about the type of treatment and identifying patients at risk of a poor outcome.

The objective of this thesis was to describe the clinical course of chronic non-specific low back pain in patients referred to a rehabilitation centre in tertiary care, to identify prognostic factors for recovery, and to analyse the influence of various outcomes and statistical techniques on the development of a prognostic model. This study included 1,760 patients with chronic non-specific low back which completed a 2-month multidisciplinary treatment and were followed up at 5- and 12-months.
In summary, the clinical course of patients with chronic non-specific low back pain who did not recover during primary and secondary care seemed to improve after a rehabilitation program, with success rates up to 60% at 12-months follow-up depending on the definition of recovery.
Younger age, being female, being married or living with one adult, lower pain intensity and disabilities, higher quality of life (physical and mental) and a higher work participation increased the change for recovery.

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