Early rehabilitation after lumbar disc surgery is not effective or cost-effective compared to no referral: a randomised trial and economic evaluation

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Research

Early rehabilitation after lumbar disc surgery is not effective or cost-effective compared to no referral: a randomised trial and economic evaluation

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KEY WORDS

Rehabilitation
Exercise therapy
Intervertebral disc degeneration
Discectomy

ABSTRACT

Question: Is referral for early rehabilitation after lumbar disc surgery effective and cost-effective compared to no referral? **Design**: Multicentre, randomised, controlled trial, and economic evaluation with concealed allocation and intention-to-treat-analysis. **Participants**: Adults who underwent discectomy for a herniated lumbar disc, confirmed by magnetic resonance imaging, and signs of nerve root compression corresponding to the herniation level. **Intervention**: Early rehabilitation (exercise therapy) for 6 to 8 weeks, versus no referral, immediately after discharge. **Outcome measures**: In line with the recommended core outcome set, the co-primary outcomes were: functional status (Oswestry Disability Index); leg and back pain (numerical rating scale 0 to 10); global perceived recovery (7-point Likert scale); and general physical and mental health (SF12), assessed 3, 6, 9, 12 and 26 weeks after surgery. The outcomes for the economic evaluation were quality of life and costs, measured at 6, 12 and 26 weeks after surgery. **Results**: There were no clinically relevant or statistically significant overall mean differences between rehabilitation and control for any outcome adjusted for baseline characteristics: global perceived recovery (OR 1.0, 95% CI 0.6 to 1.7), functional status (MD 1.5, 95% CI −3.6 to 6.7), leg pain (MD 0.1, 95% CI −0.7 to 0.8), back pain (MD 0.3, 95% CI −0.3 to 0.9), physical health (MD −3.5, 95% CI −11.3 to 4.3), and mental health (MD −4.1, 95% CI −9.4 to 1.3). After 26 weeks, there were no significant differences in quality-adjusted life years (MD 0.01, 95% CI −0.02 to 0.04 points) and societal costs (MD −€527, 95% CI −2846 to 1506). The maximum probability for the intervention to be cost-effective was 0.75 at a willingness-to-pay of €32 000/quality-adjusted life year. **Conclusion**: Early rehabilitation after lumbar disc surgery was neither more effective nor more cost-effective than no referral. **Trial registration**: Netherlands Trial Register NTR3156. **[Oosterhuis T, Ostelo RW, van Dongen JM, Peul WC, de Boer MR, Bosmans JE, Vleggeert-Lankamp CL, Arts MP, van Tulder MW (2017) Early rehabilitation after lumbar disc surgery is not effective or cost-effective compared to no referral: a randomised trial and economic evaluation. *Journal of Physiotherapy* 63: 144–153]**

Introduction

Lumbosacral radicular syndrome, also called sciatica, is commonly caused by a herniated lumbar disc.[1] The syndrome is characterised by lower limb pain radiating below the knee in an area of the leg served by one or more lumbosacral nerve roots. Sometimes, there are other neurological findings such as sensory and motor deficits. The incidence of sciatica is estimated at 5 per 1000 adults in Western countries.[2] In the Netherlands, the incidence of sciatica has increased from 75 000 to 85 000 cases per year over the past decade.[3,4] The direct and indirect costs of patients suffering from sciatica approximate €1.2 billion per year.[3] The natural course of sciatica is favourable in the majority of patients;[5] therefore, international consensus is that surgical treatment should only be offered if the radiating leg pain persists despite a period of conservative management.[6] Rates of spinal surgery differ across and within countries:[7] in the United States they are 30% higher than in the Netherlands, 50 to 60% higher than in Canada, and 80% higher than in the UK.[2] It is estimated that in the Netherlands, about 12 000 operations per year are performed for herniated lumbar discs.[4] Recovery rates after conventional microdiscectomy of 66% at 4 weeks, and 75% at 8 weeks follow-up have been reported,[8] and return to work rates of 15% at 2 months follow-up.[9] A recently published systematic review concluded that even 5 years after surgery, patients still experience mild to moderate levels of pain and disability.[10]

Two common options exist for postoperative management.[11] The first option is referral for early rehabilitation immediately after discharge. The second option comprises the advice to return to an active lifestyle, with postoperative rehabilitation only for those

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patients whose symptoms persist longer than 6 to 8 weeks. A recent systematic review investigated the effectiveness of rehabilitation following lumbar disc surgery.[12] For exercise programs starting 4 to 6 weeks after surgery, there is moderate evidence that they are more effective in improving physical function, and low-quality evidence that they are more effective than no treatment in decreasing pain. Moreover, there is moderate evidence that high-intensity exercises starting 4 to 6 weeks after surgery are more effective in improving physical function than low-intensity exercises, and low-quality evidence that they are more effective in decreasing pain than low-intensity exercises. Large, high-quality studies assessing the effectiveness of immediate postoperative interventions are lacking.[12] The effectiveness of early rehabilitation has been assessed in three mono-centre studies, which included a total of 124 patients.[13–15] The first outcome measurement was at 6 weeks, showing better function in the early rehabilitation group,[13–15] but no difference in pain.[14,15] The next follow-up was at 12 weeks, showing better function but inconsistent results for pain.[13–15] As referral for rehabilitation is associated with higher healthcare costs than no referral, it is important to assess its cost-effectiveness as well. However, cost-effectiveness studies on early rehabilitation are lacking.

Therefore, the research question for this multicentre, randomised, controlled trial was:

> Is referral for early rehabilitation after lumbar disc surgery effective and cost-effective compared to no referral?

Method

Design

A multicentre, randomised, controlled trial was conducted with a 26-week follow-up period and repeated measurements within the first 12 weeks. This schedule of measurements was chosen because a change in outcomes was expected predominantly during and shortly after the first 6 postoperative weeks. Details of the design and methods of the trial have been published previously.[16]

Participants, therapists and centres

Eligible patients had a herniated lumbar disc confirmed by magnetic resonance imaging (MRI) and signs of nerve root compression corresponding to the level of disc herniation; were aged between 18 and 70 years; and were able to fill out questionnaires in Dutch themselves. Neurosurgeons referred potentially eligible patients to the research team. Research nurses checked the eligibility criteria and excluded patients if they met any of the following criteria: cauda equina syndrome, neurogenic claudication, co-morbidities of the lumbar spine (eg, fractures, carcinomas, osteoporosis), spinal surgery in the prior 12 months, contraindications to exercise therapy (eg, acute respiratory or cardiovascular complaints, acute systemic infections), pregnancy, or previous lumbar disc surgery at the same level and on the same side. To conceal treatment allocation, a computer-randomised list was generated for each hospital by an independent investigator prior to study commencement. To achieve the predetermined sample size for the experimental and control groups, weighted block randomisation (blocks of four) was used. Based on these lists and prior to the start of the study, the independent investigator prepared a set of numbered, opaque and sealed envelopes containing the assigned postoperative strategy for each hospital. Directly after having received the completed baseline questionnaire and prior to surgery, the research nurse opened the next consecutive envelope in order to inform the participant about the assigned postoperative strategy. The nature of the postoperative strategies and the use of patient-reported outcome measures precluded blinding of the participants and the therapists. Participant expectations were measured to assess a possible risk of bias due to this lack of blinding of participants. Participants were recruited from 10 peripheral hospitals that were located in urban or regional areas of three regions in the Netherlands. Primary care physiotherapists and exercise therapists in the catchment areas of these hospitals provided the early rehabilitation following lumbar disc surgery.

Intervention

During hospitalisation (usually 1 to 2 days) all participants, regardless of treatment allocation, received usual postoperative care. More specifically, during one or two sessions, a physiotherapist or nurse provided advice and instructions for transfers (eg, bed to stand, chair to stand) and performing activities of daily living, in preparation for discharge. At discharge, participants received a booklet providing advice (mainly regarding activities of daily living) and suggestions for exercises, focusing on muscle strengthening, core stability and mobilisation.

Experimental group: referral for early rehabilitation

Participants in the experimental group received a referral for postoperative exercise therapy in primary care starting the first week after discharge. Over 6 to 8 weeks, participants received one or two individual, face-to-face, exercise therapy sessions of 30 minutes per week, conforming to a standardised treatment protocol based on a national clinical guideline.[17] The 6- to 8-week period reflected the period before patients consulted their neurosurgeon again after surgery. The timing of this follow-up consultation and, therefore, the exact duration of the period until follow-up depended on the organisation in the hospital in which the participant was treated. The treatment protocol described the treatment in terms of treatment goals; the main goal of the exercise therapy was to gradually extend activities of daily living from personal care to housekeeping tasks in the short term, and return to work and prepare for sports and leisure activities in the long term. In the first week, therapists performed physical examinations, and focused treatment on the ability and possibility to execute personal care activities and perform transfers in the home situation. From the second week onwards, exercises were taught with gradually increasing intensity, targeting limitations that were found in the initial postoperative assessment. The exact type of exercises was left to the therapists' discretion, based on the outcomes of the physical examination and taking participants' preferences into account, which was in line with routine clinical practice. Therapists provided tailored advice on lifestyle and the execution of activities of daily living. Treatment could be terminated before the end of the 6- to 8-week period if the participant was fully recovered. At each treatment session, participating therapists filled out a registration form, including (amongst other information): treatment goals on both a global and more specific level; whether a home exercise regimen was prescribed or not; and, if applicable, the reason for terminating the treatment.

Control group: no referral for early rehabilitation

Participants assigned to the control group were not referred for rehabilitation after discharge from the hospital. Participants could consult their neurosurgeon or general practitioner in case of recurring or increasing complaints, but they were requested to refrain from referral for exercise therapy or other allied health interventions in the 6- to 8-week period before consulting the neurosurgeon after surgery. The research nurses limited the extent to which they provided advice when participants allocated to the control group called them. To prevent diminishing contrast between groups, only advice that had been given during the clinical phase was repeated.

Follow-up neurosurgeon consultation

Six to 8 weeks after discharge, a follow-up consultation with the neurosurgeon took place, which was in line with routine clinical practice (see above). Whether participants in the experimental group continued rehabilitation or control group participants started

rehabilitation after this follow-up consultation was left to the neurosurgeons' discretion. This continuation of rehabilitation as well as all other healthcare consumption (in both groups) was measured by cost questionnaires. Compliance with the allocated treatment and possible crossover were measured with questionnaires.

Outcome measures

Baseline assessments took place preoperatively, and follow-up measurements at 3 days (pain intensity only) and at 3, 6, 9, 12 and 26 weeks after surgery. The study used standardised instruments with demonstrated validity, reliability and responsiveness, as detailed below. Outcomes were measured centrally using online questionnaires, but postal questionnaires were available if requested. The baseline measures included demographic data (such as age, gender and education), relevant prognostic factors and primary outcomes.

Prognostic factors

Prognostic factors, indicating an unfavourable outcome after lumbar disc surgery, included duration of symptoms and medication use preceding surgery, and complications during surgery, which were measured at baseline.[18] Also at baseline, scores were obtained on the following instruments: credibility/expectancy questionnaire,[19] the Örebro Musculoskeletal Pain Screening Questionnaire,[20] the Fear-Avoidance Beliefs Questionnaire,[21] and the Pain Coping Inventory.[22]

Co-primary outcomes

Following the recommended core set of outcomes for low back pain research,[23] all (self-reported) outcomes were selected based on the rationale and the main aims of the exercise therapy. Functional status was assessed by the Oswestry Disability Index (version 2.1.a).[24] Average pain intensity over the preceding week was measured for leg pain and low back pain on an 11-point numerical rating scale (0 = no pain to 10 = worst imaginable pain).[25] Global perceived effect was evaluated using the seven-point Global Perceived Effect scale, ranging from 'completely recovered' to 'worse than ever'. This was dichotomised into success (completely and much recovered) and non-success (slightly recovered, no change, slightly worse, much worse and worse than ever). General physical and mental health were assessed with the Medical Outcome Study Short Form 12 (SF-12).[26] For the cost-effectiveness analysis, the EuroQol (EQ-5D-3L) was administered to assess health-related quality of life.[27,28] This instrument evaluates five health dimensions on a three-point scale (no problems, moderate problems, and severe problems).

Cost measures and utility scores

Cost data were collected from a societal perspective at 6, 12 and 26 weeks after surgery using cost questionnaires. All costs related to leg and back pain were considered. These included intervention, healthcare, informal care, absenteeism, and unpaid productivity costs. Intervention costs were estimated based on the total number of physiotherapy and/or exercise therapy sessions the participant received during the period to the first follow-up (ie, 6 weeks). Healthcare costs included primary and secondary healthcare costs valued using Dutch standard costs.[29] If unavailable, prices according to professional organisations were used. Both prescribed and over-the-counter medication use was valued using unit prices of the Royal Dutch Society of Pharmacy.[30] Informal care was valued using a Dutch shadow price of €13.74/hour.[29] A modified version of the Productivity and Disease Questionnaire was used to measure absence from paid work.[31] Absenteeism costs were valued according to the friction cost approach,[32] using the estimated price of productivity losses per sickness absence day in the Netherlands based on 5-year age categories and gender.[29] The friction cost approach assumes that costs are limited to the period needed to replace a sick worker (ie, the friction period, which is estimated to be 23 weeks in the Netherlands).[32] Productivity losses from unpaid work (ie, all hours of volunteer work, and domestic and educational activities that participants were not able to perform due to their leg and back pain) were valued using a Dutch shadow price.[32] Appendix 1 presents an overview of the cost prices used for valuing resource use (see eAddenda). All costs were converted to 2014 euros using consumer price indices.[33] Because of the 26-week time horizon, discounting of costs was not necessary. Utilities based on the EuroQol (EQ-5D-3L) were estimated using the Dutch tariff.[28] Quality-adjusted life years (QALYs) were calculated using linear interpolation between measurement points. Details of the statistical analysis plan available in Appendix 2 and the code used to conduct the analyses in the statistical software are presented in Appendix 3 (see eAddenda).

Data analysis

Sample size calculations were based on a Cochrane review assessing the effectiveness of rehabilitation following lumbar disc surgery,[34] and were performed for the three main outcomes (for all: power 0.9, alpha 0.05, two-tailed test). To detect clinically relevant mean differences in a multi-level analysis, the following numbers of participants were needed: 165 participants for an 8-point difference on the Oswestry Disability Index, 105 participants for a 2-point difference on the NRS, 150 participants for a 20% difference on the dichotomised Global Perceived Effect Scale. Anticipating 15% potential study withdrawal, 200 participants were needed, with an unequal number per group (109 experimental versus 91 control) taking into account the multilevel structure of the data in the experimental group. Analyses of effectiveness and cost-effectiveness were performed using STATA[a].

Analyses of effectiveness

Baseline characteristics in both groups were compared to check prognostic comparability. The primary analysis was an intention-to-treat analysis. All continuous outcomes were analysed in a linear mixed model with responses at baseline, 3, 6, 9, 12 and 26 weeks. In these analyses, the levels of hospital, therapist, participant, and time of measurement were taken into account. Log likelihood ratios of naïve models were compared with models including an intercept for hospital or therapist. Time-by-treatment interactions were tested. Overall mean differences were presented or mean differences per time point in the case of significant time-by-treatment interactions. Regression coefficients with 95% CI signifying differences between baseline and follow-up measurements were estimated. Analyses were adjusted for confounders, defined as variables that changed the regression coefficient by $\geq$10%. For the dichotomous outcomes, a generalised mixed model (logit link) with the same multilevel structure was used. Odds ratios with 95% CI were calculated. A per-protocol analysis was performed to estimate the extent to which protocol deviations influenced the results. A protocol deviation was defined as receiving one or more sessions of exercise therapy in the first 6 to 8 weeks after surgery in the control group, or not receiving any sessions of exercise therapy in the first 6 to 8 weeks after surgery by participants in the experimental group.

Analyses of cost-effectiveness

A cost-utility analysis was performed according to intention-to-treat from a societal perspective. Using multivariate imputation by chained equations (MICE) with predictive mean matching, 10 complete data sets were created (loss-of-efficiency $<$5%).[35] The imputation model consisted of variables differing between groups at baseline and between respondents with and without complete follow-up, and variables associated with the outcomes. Analyses were performed on all 10 separate complete datasets and pooled estimates were estimated according to Rubin's rules.[35] Mean between-group cost differences were calculated for total and disaggregated costs. Seemingly unrelated regression analyses were performed to estimate total cost and QALY differences while adjusting for confounders and taking into account the possible

correlation between costs and effects. Incremental cost-effectiveness ratios were calculated by dividing the adjusted difference in total costs by the adjusted difference in QALYs. Bias-corrected and accelerated bootstrapping with 5000 replications was used to estimate the uncertainty surrounding the cost differences and incremental cost-effectiveness ratios. The latter was graphically presented in a cost-effectiveness plane.[36] A cost-effectiveness acceptability curve was estimated to indicate the intervention's probability of cost-effectiveness compared with control at different values of willingness-to-pay.[37] Three sensitivity analyses were performed: a complete-case analysis; estimation of QALYs using the SF-12 and the tariff of Brazier et al;[38] and a per-protocol analysis.

Results

Flow of participants, therapists and centres through the study

From May 2012 to December 2014, 356 patients were referred to the research team and, of those, 172 were not included for various reasons (Figure 1). Of the remaining 184 participants, 10 recovered before surgery could be performed and one participant did not undergo surgery because immediate angioplasty was required for an acute vascular complication unrelated to the disc herniation. Of the 173 participants who underwent surgery, four were excluded due to cauda equina syndrome (n = 2), carcinoma (n = 1), and decompression for stenosis (n = 1).

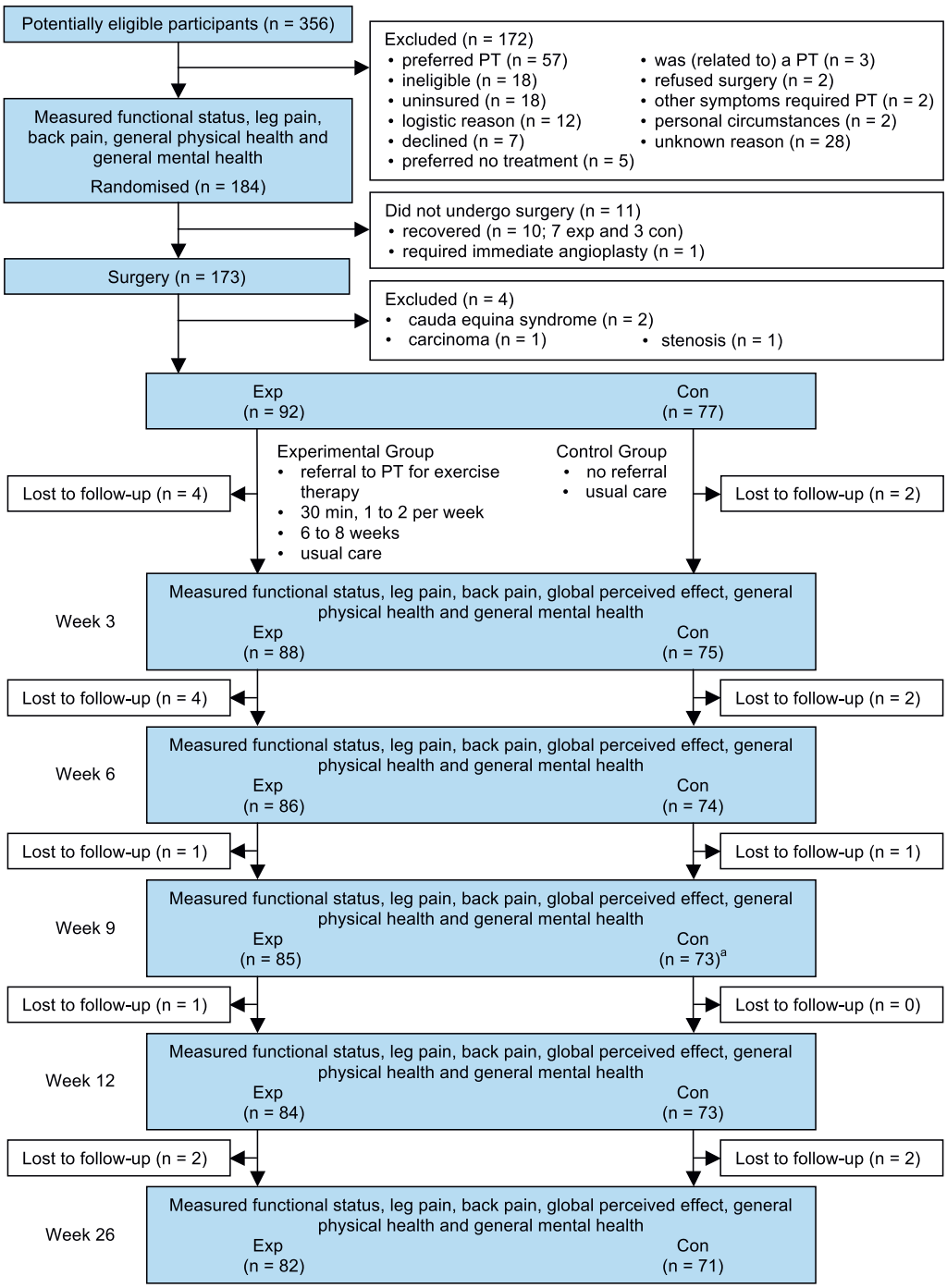

Figure 1. Design and flow of participants through the trial. PT = physiotherapist.
[a] Two participants had missing measurements at this time point but were not lost to follow-up.

Is referral for early rehabilitation after lumbar disc surgery (experimental) effective and cost-effective compared to no referral (control)?

Baseline characteristics of the experimental (n = 92) and control (n = 77) group are presented in Table 1. Baseline measures were taken a mean of 13 days (SD 15) before surgery. The groups were well matched with respect to demographic characteristics and baseline values of the outcome measures. Complete data were available from 88% and 87% of the participants in rehabilitation and control group on the effect measures, and from 80% and 74% on the cost measures, respectively.

For 51 participants (55%) in the rehabilitation group, registration forms were obtained from the treating therapists. The reported aims of the treatment were primarily focused on stabilisation and coordination (73% of the sessions), mobility (72%), strength (66%), endurance (54%), and instructions regarding lifestyle and posture (45%). Therapists prescribed home exercises in 91% of the sessions. For 41% of the participants, treatment was ended at 6 to 8 weeks after surgery because treatment goals were reached. At the 6-week follow-up, participants in the experimental group reported having received on average 6.5 treatment sessions (SD 3.7).

Co-interventions during the first 6 weeks were limited, did not greatly differ between the groups and included (experimental versus control): visit to an occupational physician 35% versus 31%, visit to a general practitioner 21% versus 17%, > 1 visit to a neurosurgeon 9% versus 4%, other allied health professional 3% versus 1%, and complementary/alternative health professional 1% versus 4%. Healthcare utilisation during the 26 weeks of follow-up included (experimental versus control): radiograph 2% versus 4%, MRI 8% versus 7%, revision surgery 3% versus 5%, physiotherapy or exercise therapy after 6 weeks 57% versus 31%.

In the intention-to-treat analysis, log likelihood ratios of naïve models and models including an intercept for hospital were equal. Furthermore, five therapists treated two participants each and all other therapists treated one participant each. Hospital and therapist were, therefore, not included as a level in the mixed model analyses. Interaction terms for time by treatment were not significant, and therefore not included. Multilevel analyses showed no clinically relevant or statistically significant overall mean differences between groups on any outcome (Table 2). Individual participant data are presented in Appendix 4 (see eAddenda). Recovery rates for the rehabilitation and control group, respectively, were 59% and 57% at 3 weeks, 70% and 69% at 6 weeks and then plateaued, except for a temporarily increased recovery at 12 weeks in the control group. A similar pattern of early decrease in pain and increase in functional status was seen in both groups.

In the experimental group, six participants (7%) did not receive any treatment by a physiotherapist or exercise therapist. Seven participants (9%) in the control group received physiotherapy during the first 6 weeks after surgery. Therefore, the per-protocol analysis included 156 participants. Baseline characteristics were largely similar to the intention-to-treat analysis, and multilevel analyses showed no relevant or statistically significant differences between groups on any outcome (data not shown).

The between-group difference in QALYs was not significant. Total societal costs in the rehabilitation group were lower than in the control group, but this difference was not statistically significant (–€527, 95% CI –2846 to 1506) (Table 3). Disaggregate costs that were significantly higher in the rehabilitation group than in the control group included intervention costs (€257, 95% CI 226 to 295) and primary care costs (€364, 95% CI 71 to 630). The control group had higher costs for informal care (–€602, 95% CI –1582 to –172) and unpaid productivity (–€449, 95% CI –1005 to –132). Absenteeism costs were the largest contributor to total societal costs in both groups, but did not differ significantly between the groups. The incremental cost-effectiveness ratio was –85 394, indicating that the intervention saved €85 394 per QALY gained (Table 4). The cost-effectiveness pairs were scattered around the four quadrants of the cost-effectiveness plane, indicating a high level of uncertainty around the estimates (Figure 2a). The cost-effectiveness acceptability curve indicated that if society was not willing to pay anything per QALY gained, the probability of cost-effectiveness was 0.73 (Figure 2b). This probability only marginally increased to a maximum of 0.75, at a willingness to pay of €32 000/QALY. The results of the three sensitivity analyses did not substantially differ from the main analysis (Table 4).

Table 1
Baseline characteristics of the participants.

Characteristic	Exp (n = 92)	Con (n = 77)
Age *(yr)*, mean (SD)	47 (12)	47 (12)
Female, n (%)	54 (59)	44 (57)
Living alone, n (%)	16 (16)	8 (10)
Education, n (%)		
low	20 (22)	17 (22)
middle	47 (51)	35 (45)
high	25 (27)	25 (32)
Employed, n (%)	74 (80)	57 (74)
Level of herniation, n (%)		
L2 to 3	1 (1)	2 (3)
L3 to 4	10 (11)	4 (5)
L4 to 5	31 (34)	42 (58)
L5 to S1	48 (52)	29 (38)
L5 to 6	1 (1)	2 (3)
Type of herniation, n (%)		
sequestered	34 (37)	34 (44)
bulging disc	57 (62)	46 (60)
extraforaminal	1 (1)	2 (3)
Functional status *(ODI, 0 to 100)*, mean (SD)	48.6 (17.3)	50.4 (15.6)
Pain intensity *(NRS, 0 to 10)*, mean (SD)		
leg	7.8 (1.9)	7.7 (1.8)
back	6.5 (2.5)	6.1 (2.6)
General physical health *(SF12, 0 to 100)*, mean (SD)	26.2 (16.1)	26.7 (15.4)
General mental health *(SF12, 0 to 100)*, mean (SD)	51.6 (21.5)	50.3 (21.8)
Psychosocial status *(ÖMPSQ, 0 to 210)*, mean (SD)	109.0 (24.9)	114.2 (20.5)
Fear avoidance beliefs *(FABQ, 0 to 24)*, mean (SD)		
physical activity	16.1 (4.4)	15.4 (5.4)
work	16.8 (11.0)	18.5 (11.3)
Expectations: *(CEQ, 3 to 27)*, mean (SD)		
expectancy surgery	23.2 (2.8)	22.9 (3.0)
credibility surgery	22.0 (3.2)	21.7 (3.7)
Expectations: credibility item *(CEQ, 1 to 9)*, mean (SD)		
experimental	6.5 (1.8)	6.3 (1.8)
control	6.4 (1.6)	6.5 (1.4)
Pain coping: active *(PCI)*		
active	6.7 (1.3)	6.5 (1.3)
passive	6.5 (1.3)	6.5 (1.2)
Duration of complaints *(months)*, n (%)		
0 to 1	2 (2)	0 (0)
1 to 2	6 (7)	3 (4)
2 to 3	1 (1)	7 (9)
3 to 6	35 (38)	29 (38)
6 to 9	18 (20)	13 (17)
9 to 12	6 (7)	7 (9)
>12	24 (26)	18 (23)
Medication use, n (%)		
every day	56 (61)	47 (61)
not every day	18 (20)	14 (18)
no	18 (20)	16 (21)
Surgical complications, n (%)		
nerve root injury	1 (1)	1 (1)
dural tear	2 (2)	2 (3)
increase in sensimotor deficit	0 (0)	1 (1)

Percentages may not tally to 100%, due to rounding.
CEQ = credibility/expectancy questionnaire, FABQ = Fear-Avoidance Beliefs Questionnaire, NRS = numerical rating scale, ODI = Oswestry Disability Index, ÖMPSQ = Örebro Musculoskeletal Pain Screening Questionnaire, PCI = Pain Coping Inventory, SF12 = Medical Outcome Study Short Form 12.

Discussion

Early rehabilitation after lumbar disc surgery had no significant effect on any clinical outcome, QALYs or societal costs in comparison with no referral for early rehabilitation. In both

Table 2
Clinical outcomes.

Outcome	Exp (n = 92)	Con (n = 77)	Mean difference (95% CI)
Functional status *(ODI, 0 to 100)*			
baseline	48.6 (17.3)	50.4 (15.6)	
3 weeks	29.5 (18.9)	29.6 (19.0)	
6 weeks	20.3 (16.2)	18.9 (16.9)	
9 weeks	16.6 (16.9)	15.2 (17.1)	
12 weeks	15.4 (15.6)	13.5 (17.0)	
26 weeks	14.3 (16.6)	14.3 (18.0)	
			crude 1.0 (−3.7 to 5.7)
			adjusted 1.5 (−3.6 to 6.7)[a]
Pain intensity leg *(NRS, 0 to 10)*			
baseline	7.8 (1.9)	7.7 (1.8)	
3 weeks	2.7 (2.9)	3.1 (3.0)	
6 weeks	2.1 (2.5)	2.1 (2.5)	
9 weeks	1.8 (2.5)	2.1 (2.7)	
12 weeks	2.0 (2.7)	1.8 (2.6)	
26 weeks	2.0 (2.7)	2.0 (2.7)	
			crude −0.1 (−0.8 to 0.6)
			adjusted 0.1 (−0.7 to 0.8)[b]
Pain intensity back *(NRS, 0 to 10)*			
baseline	6.5 (2.5)	6.1 (2.6)	
3 weeks	3.5 (2.4)	3.3 (2.4)	
6 weeks	2.8 (2.1)	2.8 (2.3)	
9 weeks	2.8 (2.5)	2.2 (2.4)	
12 weeks	2.9 (2.5)	2.4 (2.5)	
26 weeks	2.8 (2.4)	2.5 (2.6)	
			crude 0.3 (−0.3 to 0.9)
			adjusted 0.3 (−0.3 to 0.9)[c]
Global perceived effect, n (%) recovered			
3 weeks	54 (59)	44 (57)	
6 weeks	64 (70)	53 (69)	
9 weeks	61 (66)	53 (69)	
12 weeks	62 (67)	60 (78)	
26 weeks	60 (65)	50 (65)	
			OR 1.0 (0.6 to 1.7)
General physical health *(SF12, 0 to 100)*			
baseline	26.2 (16.1)	26.7 (15.4)	
3 weeks	38.2 (22.3)	36.5 (23.7)	
6 weeks	47.9 (26.3)	48.7 (26.2)	
9 weeks	53.5 (29.6)	54.3 (31.0)	
12 weeks	57.8 (30.2)	62.2 (33.4)	
26 weeks	63.0 (31.8)	63.0 (34.5)	
			crude −1.1 (−8.5 to 6.3)
			adjusted −3.5 (−11.3 to 4.3)[d]
General mental health *(SF12, 0 to 100)*			
baseline	51.6 (21.5)	50.3 (21.8)	
3 weeks	58.1 (21.7)	61.2 (22.6)	
6 weeks	70.0 (21.8)	71.7 (22.1)	
9 weeks	73.9 (20.2)	73.1 (23.5)	
12 weeks	77.4 (21.0)	78.5 (23.3)	
26 weeks	77.6 (20.8)	76.1 (23.0)	
			crude −0.9 (−6.8 to 5.0)
			adjusted −4.1 (−9.4 to 1.3)[e]

Data are mean (SD) unless stated otherwise.
NRS = numerical rating scale, ODI = Oswestry Disability Index, SF12 = Medical Outcome Study Short Form 12.
[a] Adjusted for functional status at baseline, age, gender, employment, back pain, general mental health, psychosocial profile, fear avoidance, expectancy and credibility surgery, credibility rehabilitation.
[b] Adjusted for leg pain at baseline, living status, employment, psychosocial profile, general mental health, fear avoidance, expectancy and credibility surgery.
[c] Adjusted for back pain at baseline, psychosocial profile, fear avoidance, expectancy surgery.
[d] Adjusted for general physical health at baseline, age, living status, functional status, back pain, general mental health, psychosocial profile, fear avoidance, expectancy surgery, credibility rehabilitation and watchful waiting, pain coping.
[e] Adjusted for general mental health at baseline, age, living status, employment, functional status, back pain, general physical health, psychosocial profile, fear avoidance, credibility and expectancy surgery, credibility rehabilitation and watchful waiting, pain coping.

groups, the main decrease in pain and increase in functional status scores were obtained in the first weeks after surgery. The highest probability of the intervention being cost-effective compared with control was 0.75, at a willingness-to-pay of € 32 000/QALY. The results of the sensitivity analyses were in line with the main analysis, indicating that the findings were robust. Based on these findings, early rehabilitation after lumbar disc surgery cannot be considered effective or cost-effective in comparison with no referral.

The pragmatic randomised, controlled trial design was an important strength of the present study, as it allowed for evaluation of the intervention's effectiveness and cost-effectiveness in a real world situation and prospective collection of outcome data including cost data. Ten hospitals and many therapists were involved, which enhances the generalisability of the findings. Using randomisation, measurement instruments recommended in the core outcome set, and the low dropout rate guaranteed the internal validity. Still, this study also had a few limitations. First, due to the nature of the intervention, participants and care providers could not be blinded. However, participant expectations (ie, credibility scores for both experimental and control) were similar in both groups. Therefore, a lack of blinding does not seem to have had much impact on the results. Second, baseline measures and randomisation took place before surgery for logistic reasons

Table 3
Mean cost per participant in the experimental and control group, and mean cost differences between groups during the 26 weeks of follow-up.

Cost category	Cost per participant, (€) mean (SEM)		Cost difference, (€) mean (95% CI)	
	Exp (n = 92)	Con (n = 77)	crude	adjusted
Intervention costs	257 (16)	0 (0)	257 (228 to 290)	257 (226 to 295)
Medical costs	1240 (117)	997 (192)	243 (−217 to 639)	241 (−205 to 688)
primary care	1046 (96)	652 (131)	394 (77 to 677)	364 (71 to 630)
secondary care	172 (67)	308 (117)	−136 (−454 to 92)	−108 (−402 to 143)
medication	22 (8)	37 (13)	−15 (−48 to 10)	−15 (−48 to 9)
Informal care costs	375 (74)	987 (334)	−611 (−1817 to −165)	−602 (−1582 to −172)
Absenteeism costs	4404 (559)	4113 (718)	291 (−1629 to 1967)	27 (−1707 to 1591)
Unpaid productivity costs	209 (67)	693 (211)	−484 (−1108 to −157)	−449 (−1005 to −132)
Total	6486 (626)	6790 (957)	−304 (−2812 to 1765)	−527 (−2846 to 1506)

Table 4
Differences in pooled mean costs and effects (95% CI), incremental cost-effectiveness ratios, and the distribution of incremental cost-effect pairs around the quadrants of the cost-effectiveness planes.

Analysis	n		Difference in costs (€)	Difference in QALYs	ICER (€/point)	Distribution CE-plane (%)			
	Exp	Con	(95% CI)	(95% CI)		NE[a]	SE[b]	SW[c]	NW[d]
Main[e]	92	77	−678 (−3048 to 1357)	0.01 (−0.02 to 0.04)	−85394	13.2	55.3	17.7	13.8
Sensitivity									
1[f]	74	57	−515 (−3396 to 1749)	−0.00 (−0.03 to 0.03)	1458267	9.8	23.9	39.9	26.3
2[g]	92	77	−637 (−3002 to 1381)	0.001 (−0.006 to 0.008)	−625531	22.7	40.0	32.5	4.8
3[h]	86	70	−329 (−2760 to 1738)	0.01 (−0.02 to 0.04)	−34438	22.7	50.0	10.7	16.6

CE = cost-effectiveness, ICER = incremental cost-effectiveness ratio, QALYs = quality-adjusted life years, which are measured on a scale from 0 to 1.
[a] Refers to the northeast quadrant of the CE-plane, indicating that early rehabilitation is more effective and more costly than no referral for early rehabilitation.
[b] Refers to the southeast quadrant of the CE-plane, indicating that early rehabilitation is more effective and less costly than no referral for early rehabilitation.
[c] Refers to the southwest quadrant of the CE-plane, indicating that early rehabilitation is less effective and less costly than no referral for early rehabilitation.
[d] Refers to the northwest quadrant of the CE-plane, indicating that early rehabilitation is less effective and more costly than no referral for early rehabilitation.
[e] Main analysis using imputed dataset.
[f] Sensitivity analysis 1 was a complete case analysis.
[g] Sensitivity analysis 2 involved estimation of QALYs using the SF-12 questionnaire[25] and the tariff of Brazier et al.[37]
[h] Sensitivity analysis 3 was a per-protocol analysis.

(ie, treatment started a few days after surgery) and to prevent participants' uncertainty during and after hospitalisation about the postoperative management. Eleven participants did eventually not receive surgery and were, therefore, withdrawn. Besides, as Fergusson et al suggested, excluding these prematurely randomised participants does not bias the analysis if treatment allocation is not associated with the likelihood of undergoing surgery.[39] Participants in both arms declined surgery (control n = 3, experimental = 7) due to recovery. There is no reason to assume that recovery before surgery could be performed is associated with group allocation. Third, the study relied on self-reported cost data. Health insurance claim data and sickness absence data are practically inaccessible in the Netherlands, as it requires the cooperation of over 30 different insurance companies and employers of all employed participants. Moreover, data for informal and uninsured care are not registered at all by these companies. However, closed questions were used to measure costs over periods of 1.5 to 3 months. As closed questions have been found to be reliable for recall periods up to 6 months,[40] it was not expected that recall bias would be an important issue. Besides, any recall bias (for absenteeism or healthcare costs) was likely to have affected both groups equally. Finally, a potential limitation of the study was that multiple co-primary outcomes were nominated, which might have inflated the risk of a Type-I error. On the other hand, all these a priori selected outcome domains are included in the recommended core set for low back pain trials,[23] as all of them are considered to be important. Moreover, it is believed that a trial has to be interpreted in light of all the available evidence, based on the apriori selected co-primary outcomes. Furthermore, in the present study, no statistically significant effects were identified on any of these outcomes. This consistency strengthened the conclusion that was drawn based on the study results.

The rationale for the intervention in the current study was that early rehabilitation aimed at resumption of daily activities prescribed to all patients might accelerate recovery, including return to work. However, this was not found in the current trial. The predominantly early decrease in pain and increase in functional status without relevant between-group differences was also reported in earlier trials that compared rehabilitation with no treatment starting 1 week,[15] or 6 weeks after surgery.[41] The present results strengthen the conclusion of the Cochrane review of rehabilitation after lumbar disc surgery,[12] which found very limited evidence of no difference between rehabilitation programs starting immediately after surgery and no rehabilitation, because only one low-quality, randomised, controlled trial was available (ie, the trial by Ju et al[42]). Another recently published review that focused on the effectiveness of physical therapy starting within the first 4 weeks after surgery concluded that early physiotherapy leads to a moderate, statistically significant reduction in pain compared to the control group.[43] Methodological differences (eg, the Cochrane review[12] only included randomised, controlled trials while Snowdon[43] also included controlled clinical trials), differences in interpretation regarding the starting point of treatment, and differences in the interpretation of the content of the control group may explain these differences. Snowdon et al,[43] for example, argued that the randomised, controlled trial of Erdogmus et al[44] could also be included (in addition to the aforementioned trial of Ju et al[42]) in the comparison 'treatment starting immediately after surgery versus no treatment' of the Cochrane review. If this was done, and the present study was also included, three randomised, controlled trials could be included in a meta-analysis for this

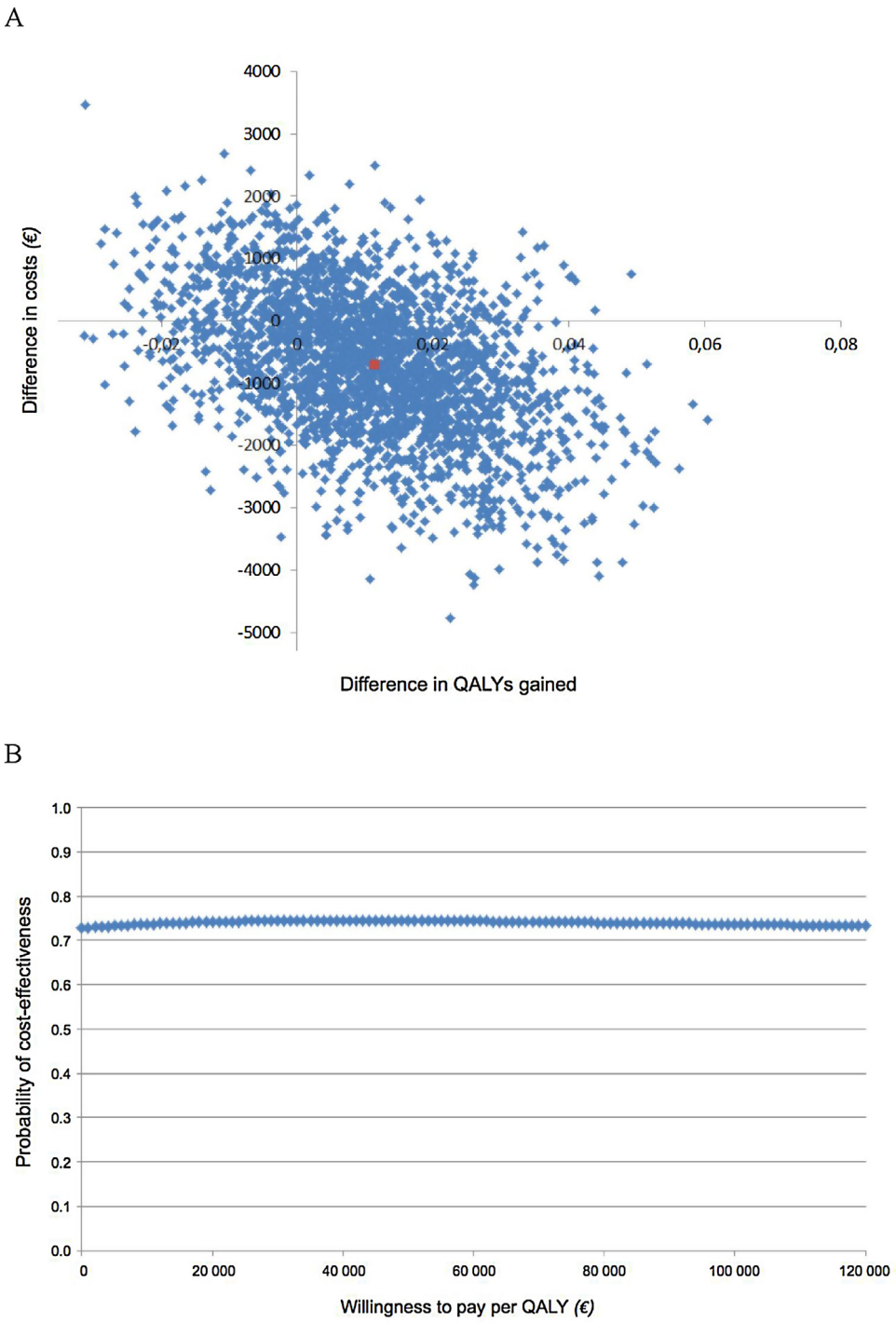

Figure 2. Cost-effectiveness planes indicating the distribution of incremental cost-effect pairs around its four quadrants (A) and cost-effectiveness acceptability curves indicating the probability of early rehabilitation being cost-effective in comparison with no referral for early rehabilitation for different values (€) of willingness-to-pay per QALY (B).

comparison (ie, Ju et al,[42] Erdogmus et al[44] and the present study). The pooled SMD (random effects model) would be –0.34 (95% CI –1.04 to 0.36). In sum, it is believed that the evidence illustrates that early rehabilitation has no added value in comparison to no treatment.

One potential explanation for the findings of this study is that the combination of careful selection of patients who may benefit from surgery by the spinal surgeon and the predominantly minimal invasive procedures (ie, microsurgery) led to a situation in which the participants, in general, were only mildly affected in the immediate postoperative period and, consequently, patients were able to resume their daily activities rather quickly. Another explanation may be that, although the current trial aimed to investigate an early rehabilitation program with a strong focus on the activities of daily living needs of the individual participant, the intervention under study might have been too generic. Based on the registration forms, the content of the treatment seemed to deviate from the protocol, with a focus on isolated exercises rather than the resumption of activities of daily living. As a consequence, the intervention under study might have been too generic instead of specifically focusing on the activities of daily living needs of the individual participant, and this may have influenced its effectiveness. Although 50% of the registration forms were received, it is thought that this description of the intervention under study is rather representative, as the main reason for not returning the registration forms by the therapists was practical (eg, no time in busy daily practice). On the other hand, as insight into the mechanisms of recovery is limited, the use of a more specific program targeting these mechanisms is hampered. It is unclear which subgroups, if any, may benefit most from postoperative

rehabilitation. Further research may contribute to the clarification of mechanisms of recovery and identifying subgroups, and subsequently designing potentially effective interventions for those with residual complaints, which could then be tested in further trials. An interesting finding in that respect is that interventions more specifically targeting mechanisms of pain chronification may be more effective, as persistent post-surgical pain may be associated with central changes in pain processing, and related to comorbid chronic pain.[45] Pain education prior to lumbar disc surgery led to far less utilisation of healthcare.[46] There were no clinically relevant differences in pain and function compared to usual preoperative care. Further research could focus on combining preoperative pain education with postoperative rehabilitation for those with persisting pain at 6 to 8 weeks only. This potentially optimises outcomes after lumbar disc surgery and reduces healthcare utilisation.

The only other cost-effectiveness study,[47] alongside a trial comparing postoperative rehabilitation to no treatment,[41] did not find significant differences in costs and effects either. However, the intervention in that study started 8 weeks after surgery. The cost-effectiveness acceptability curve of that study showed that the probability of cost-effectiveness increased with an increasing willingness-to-pay to approximately 0.52 at a ceiling ratio of £50 000/QALY (approximately €60 000),[47] which is lower than in the present study. The study included both patients with lumbar disc herniation and patients with stenosis, and reported that inpatient nights were the largest contributor to total costs. Morris et al[47] did not assess work absenteeism, whereas this was the main cost driver in the present study. The present results confirmed findings of an earlier Dutch trial on rehabilitation after discectomy, which found absenteeism to be the largest contributor to total costs.[48] To reduce these high costs, it is of utmost importance to develop interventions that effectively speed up return to work after surgery. A rehabilitation-oriented approach in insurance medicine effectively increased return-to-work rates compared to usual care insurance medicine in patients who underwent lumbar disc surgery.[49] In this intervention, starting 6 weeks postsurgery, a medical adviser coordinated a multidisciplinary approach, including all relevant healthcare providers, to achieve early return to work. Future research might, therefore, focus on investigating the cost-effectiveness of similar multidisciplinary interventions that specifically aim at an early return to work.

In conclusion, rehabilitation after lumbar disc surgery starting immediately after hospital discharge was neither effective nor cost-effective, compared to no referral for early rehabilitation. Participants in both groups improved more or less equally after surgery and early rehabilitation had no additional effect on pain, functional status, global perceived effect scale, general physical or mental health, or costs.

What is already known on this topic: The natural course of sciatica is favourable in the majority of patients, so surgery is only offered if the radiating leg pain persists despite a period of conservative management.
What this study adds: In this study, usual postoperative care involved a physiotherapist or nurse providing instructions for transfers (eg, bed to stand), advice about performing activities of daily living, and a booklet containing advice (mainly regarding activities of daily living) and suggestions for exercises, focusing on muscle strengthening, core stability and mobilisation. Where such usual care is provided, adding a referral for additional exercise-based rehabilitation with a physiotherapist (one to two sessions per week for 6 to 8 weeks) is neither effective nor cost-effective.

Footnotes: [a]STATA V.12, Stata Corp, College Station, USA.

eAddenda: Appendices 1, 2, 3 and 4 can be found online at http://dx.doi.org/10.1016/j.jphys.2017.05.016.

Ethics approval: The Medical Ethics Review Board of the VU University Medical Centre approved the study protocol (NL35897.029.11) in September 2011. Subsequently, local review boards of all participating hospitals approved the protocol. All participants gave written informed consent before data collection began.

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