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**THE CLINICAL EFFECTIVENESS AND
COST-EFFECTIVENESS OF A BEHAVIORAL
GRADED EXERCISE THERAPY PROGRAMME
FOR PATIENTS WITH CHRONIC
SHOULDER COMPLAINTS IN PRIMARY CARE**

The clinical effectiveness and cost-effectiveness of a behavioral Graded Exercise Therapy programme for patients with chronic shoulder complaints in primary care - Jacques Geraets – Thesis Maastricht University – with references – with summary in Dutch

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PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit Maastricht,
op gezag van de Rector Magnificus,
Prof. mr. G.P.M.F. Mols,
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen
op donderdag 9 maart 2006 om 16.00 uur

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CHAPTER 1

General introduction

SHOULDER COMPLAINTS

Definition

Shoulder complaints involve pain and stiffness located in the deltoid region and upper arm (van der Heijden 1999). They often cause problems when patients are lying on the affected side, and patients may be limited in the performance of daily activities relating to personal hygiene, work, hobby and sports (Croft et al 1996, van der Windt et al 1996). In addition to causing personal suffering, shoulder complaints impose an enormous social and economic burden due to patients' inability to manage their household, loss of productivity, sick leave and utilisation of health care resources (Meerding et al 1998). In this thesis, shoulder complaints are defined as chronic if they last for at least three months.

Occurrence and course

Shoulder complaints are a relatively common disorder in view of their occurrence, course and persistence. Reported prevalence rates and incidence rates of shoulder complaints vary greatly, depending on the definition used in terms of location and duration of pain and limited movements (Luime et al 2004a). The one-year period prevalence of shoulder complaints in the Dutch general population aged 25 years and older has been estimated at 30% (Picavet et al 2003). The annual prevalence of chronic shoulder complaints in this population was 15%. Forty-one percent of these patients with shoulder complaints had visited a general practitioner because of shoulder complaints in the past 12 months. Patients who consult their general practitioner for neck-shoulder complaints have greater risks of long-term pain and disability than non-consulters (Badcock et al 2003). The annual cumulative incidence of shoulder complaints recorded in general practices in the Netherlands has been reported to be as much as 25 per 1000 patients (Sobel et al 1996). Approximately 50% of all patients who visit their general practitioner with a new episode of shoulder complaints report persistent complaints after six months, and up to 40% endure complaints up to 12 months (Windt et al 1996, Winters et al 1997, Winters et al 1999a). Forty-six percent of these patients report previous episodes. Recurrence rates for shoulder complaints vary from 31% (after 12 months) to 85% (after 12 years) (Luime et al 2004b, Macfarlane et al 1998a, Andersson 2004).

Costs of shoulder complaints

The economic burden of shoulder complaints can be assessed in terms of the direct health care costs (e.g. costs of utilisation of health care services and prescribed medication), non-direct health care costs (e.g. costs of home care, housekeeping or out-of-pocket expenses) and indirect costs (e.g. loss of productivity or absenteeism from paid or unpaid work). In the Netherlands, musculoskeletal disorders, of which shoulder complaints constitute the second largest group after low back pain, also account for the second largest share in healthcare costs (Picavet et al 2003, Meerding et al 1998). In low back pain patients indirect costs far exceed the direct costs and most expenses (more than 80%) are incurred for a minority of patients (less than 25%) in whom low back pain develops into a chronic disorder (Goossens et al 1997). Musculoskeletal disorders are the main reasons for work-related consultations in Dutch general practice (Weevers et al 2005). In Sweden, 18% of disability payment made for musculoskeletal disorders relates to shoulder complaints (Nygren et al 1995).

Causes and prognosis

At present, there is a lack of information on the causes and prognosis of shoulder complaints. It is unclear what factors contribute to the initiation of shoulder complaints, what factors are involved in the transition from acute to chronic complaints and what factors play a role in the persistence of chronic complaints (van der Heijden 1999). In the traditional disease-oriented biomedical model, it is hypothesised that shoulder pain and disability are caused by acute or chronic injury of articular or periarticular soft tissues of the shoulder due to anatomic or biomechanical changes (Cyriax 1981). Although this model is useful when explaining the involvement of biomedical factors in pain at the onset of complaints, through straightforward somato-sensory stimulation, it only partly explains the prolonged pain and reduced performance of activities in chronic pain patients. The 'gate control theory' (Melzack and Wall 1965) broke with the traditional biomedical model of pain. It is based on the hypothesis that neurophysiological and psychological activity – ascending from peripheral sources or descending from the brain – can modulate the pathway of pain stimuli through the 'gate' located in the dorsal horn of the spine. In 1976, Fordyce hypothesised that factors involved in the persistence of pain do not have to correspond with the factors involved in its initiation (Fordyce 1976). He assumed that pain behaviour and the consequences of this behaviour determine to a large extent whether or not pain develops into a chronic pain problem. In the new bio-psychosocial model of pain, biological, psychological and social factors are closely related and involved in the development and maintenance of pain (Engel 1980, Nielson and Weir 2001, Turk et al 1997). Pain has sensory, affective and cognitive dimensions (Loeser 1980). Nowadays, there is strong evidence and general agreement that both biological and psychosocial factors are involved in chronic pain (Vlaeyen and Linton 2000, Keefe et al 2004, Pincus et al 2002). The International Association for the Study of Pain defines pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' indicating that pain is subjective (Merskey and Bogduk 1994). However, it is unclear whether and to what extent biological, psychological or social aspects are involved in the initiation and persistence of shoulder complaints. More severe long-term shoulder disability and pain seem to correlate with higher disability and pain scores at the start of the complaints, concomitant neck problems, a gradual onset and a longer duration of complaints (MacFarlane et al 1998a, Kuipers et al 2004, Thomas et al 2005). Furthermore, there is growing evidence that both biomechanical and psychosocial factors are associated with the occurrence of work-related shoulder complaints (van der Windt et al 2000, Andersen et al 2003, Pope et al 1997, Bongers et al 2003, Harkness et al 2003).

MANAGEMENT OF SHOULDER COMPLAINTS IN PRIMARY CARE

Usual care

In the Netherlands, the general practitioner is the gatekeeper in the professional management of patients with shoulder complaints, and is responsible for usual care and referrals to physicians and paramedical therapists. Usual care mainly focuses on pain relief and the treatment of disability in patients with shoulder complaints. Traditionally, usual care was based on signs and diagnostic classifications of shoulder complaints as described by Cyriax (Cyriax 1981). The first clinical guidelines for shoulder complaints of the Dutch College of

Table 1. Evidence for the effectiveness of commonly applied interventions for shoulder complaints in usual care

Treatment	Level of evidence	Reference
NSAIDs	Limited evidence for short-term effectiveness	van der Windt 1995
Sub-acromial or intra-articular corticosteroid injection	Limited evidence for short-term effectiveness	Aroll and Goodyear 2005, Bernstein 2001, Buchbinder et al 2003
Exercise therapy	Limited or conflicting evidence	Smit et al 2005, Desmeules et al 2003, Mior 2001a, Grant et al 2004, Michener et al 2004
Manual therapy	Limited or conflicting evidence	Mior 2001b, Bergman et al 2004
Therapeutic ultrasound	Insufficient or conflicting evidence	Robertson and Baker 2001, van der Heijden et al 1997, Michener et al 2004, van der Windt et al 1999
Electrotherapy	Insufficient or conflicting evidence	Grant et al 2004, van der Heijden 1999
Laser therapy	Insufficient or conflicting evidence	van der Heijden 1999, Michener et al 2004
Acupuncture	Insufficient or conflicting evidence	Grant et al 2004, Green et al 2005, Michener et al 2004
Open and primary surgery	Limited evidence	Grant et al 2004, Eijnsman et al 2004, Handoll et al 2004, Gibson et al 2004
Arthroscopic debridement and revision surgery	No evidence	Grant et al 2004, Lo and Burkhart 2004
Accuracy of diagnostic imaging techniques –ultrasonography, magnetic resonance imaging (MRI) or magnetic resonance arthrography (MRA) – in secondary care	Limited evidence	van der Heijden 1999, Dinnes et al 2003

General Practitioners (DCGP), issued in 1990, recommended detailed physical examination of shoulder complaints and treatment of injured soft tissues according to the Cyriax method. However, the inter- and intra-observer agreement on signs, diagnostic criteria and classifications for this method was found to be poor (Bamji et al 1996, de Winter et al 1999). Furthermore, evidence on the accuracy of clinical tests to diagnose impingement and rotator cuff tears turned out to be limited (Luime 2004c). In the revised guidelines for shoulder complaints, issued by the DCGP in 1999, the diagnostic classification system based on soft tissue pathology was replaced by a diagnostic system based on functional limitations of the shoulder girdle (Groenier et al 2003, Winters et al 1999b).

Usual care according to this revised guideline consists of information, recommendations and pain-contingent medical or drug therapy. It is the GPs who decide on the specific treatment to be administered. During the first two weeks following the initial consultation, they follow a wait-and-see policy, and give advice and information on the course of the complaints. This policy is supplemented with analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) if GPs consider them necessary. Patients are instructed to re-consult their

GP if complaints continue for more than two weeks. Up to three corticosteroid injections can then be given, or referral to a physiotherapist or specialist can be considered.

At present, there is limited evidence that biomedically based interventions speed up recovery in the short term for patients with shoulder complaints, and there is conflicting evidence on long-term effects of conservative treatment (Green 2003, van der Heijden 1999, Kroese 2002, Grin 2004). Referral of patients with shoulder pain to an orthopedic surgeon or a rheumatologist does not seem to be based on clinical signs (pain, function, duration of complaints or initial diagnosis), nor is it associated with greater improvements regarding pain and function (Solomon et al 2001). Table 1 shows the available evidence for the effectiveness of commonly applied treatments for shoulder complaints.

Behavioural treatment

Reconceptualisation of pain and the development of a new multidimensional biopsychosocial model in which biological, psychological and social factors contribute to persisting pain have led to the development of new treatments addressing psychosocial aspects in chronic pain patients (Fordyce 1976, Nielson and Weir 2001, Turk and Okifuji 1997, Flor 2003, Goucke 2003). Fordyce introduced operant conditioning principles to the management of chronic pain, focussing on the consequences of pain behaviour. Pain behaviour is thought to consolidate when patients experience the consequences of this behaviour as pleasant and to extinguish when they experience the consequences as unpleasant. Positive or negative reinforcement of the preferred behavioural changes is given to increase and maintain the desired behaviour (Fordyce 1976, Fordyce et al 1986, Lindstrom et al 1992, Turk and Okifuji 1999).

The effectiveness of cognitive-behavioural treatment programmes has been documented in several studies (Guzmán et al 2001, Morley et al 1999, Tulder et al 2001, Ostelo et al 2005, Vlaeyen and Linton 2000, Nielson and Weir 2001). However, most studies have involved combined cognitive and behavioural programmes for chronic low back pain patients, in multidisciplinary settings. Table 2 shows the available evidence for the effectiveness of behavioural treatments in musculoskeletal pain patients. It is likely that operant behavioural therapy will be effective in the treatment of patients with chronic shoulder complaints in primary care, although specific evidence on this issue is still lacking (Linton 1995).

Table 2. Evidence for the effectiveness of behavioural treatments in chronic musculoskeletal pain patients

Programme	Population	Level of evidence	Reference
Combined respondent-cognitive treatment	Low back pain	Strong evidence	Ostelo et al 2005
Progressive relaxation	Low back pain	Moderate evidence	Ostelo et al 2005
Operant-behavioural treatment	Low back pain	Limited evidence	Staal et al 2004, Ostelo et al 2005, Jensen et al 2005
Multidisciplinary biopsychosocial rehabilitation	Neck and shoulder pain	Limited evidence	Karjalainen rehabilitation et al 2001

GRADED EXERCISE THERAPY

We have developed a behavioural Graded Exercise Therapy (GET) programme, based on the principles of graded activity, time contingency and operant learning, to optimise the treatment of patients with chronic shoulder complaints in primary care. This programme is administered by a physiotherapist and attempts to improve the performance of daily activities and to reduce health care costs and indirect costs in these patients. An important aim of GET is to increase levels of daily activity by learning from the consequences of behaviours. Pain behaviour is expected to be consolidated when patients experience the consequences of this behaviour as pleasant and to extinguish when they experience it as unpleasant. Operant learning principles are used to promote and improve healthy behaviour by changing the consequences of behaviour. In graded activity, levels of activity increase in a step-wise time-contingent fashion. This means that the intensity of exercises increases gradually over time, irrespective of pain experience, towards preset goals and with fixed quota agreed upon at the start of the programme. To our knowledge, GET is the first behavioural programme to focus on patients with chronic shoulder complaints. Furthermore, GET is the first behavioural programme to be administered in a mono-disciplinary and primary care setting.

AVAILABLE EVIDENCE AT THE START OF THE STUDY

At the start of our study, there was no evidence for beneficial clinical effects of behavioural treatments in patients with chronic shoulder complaints in primary care. Nor was any evidence available on the cost-effectiveness of behavioural treatments in these patients. Finally, evidence was lacking on the feasibility of the newly developed behavioural Graded Exercise Therapy programme for patients with chronic shoulder complaints in primary care.

OBJECTIVES OF THIS THESIS

The main objective of the studies reported in this thesis was to evaluate the clinical effectiveness and cost-effectiveness of our behavioural Graded Exercise Therapy programme in patients with chronic shoulder complaints in a primary care setting. We further aimed to examine the feasibility of the GET programme and the need for improvements to the protocol to facilitate its implementation. This study was part of a research programme of the Netherlands Organisation for Scientific Research (NWO), including a comprehensive prognostic cohort study on shoulder complaints in primary care, with three randomised clinical trials on the clinical effectiveness and cost-effectiveness of three treatment modalities for shoulder complaints in subcohorts. The first trial assessed manipulative therapy of the shoulder girdle additional to usual care, while the second concerned an early education and activation programme in patients with acute shoulder complaints. The third, the present study, examined the behavioural Graded Exercise Therapy programme in patients with chronic shoulder complaints.

OUTLINE OF THIS THESIS

The following research questions are answered in the successive chapters of this thesis:

- Chapter 2 discusses the theory and the conceptual model underlying the Graded Exercise Therapy Programme. Furthermore, the development and content of the programme and the design of the study to evaluate the programme's effectiveness and cost-effectiveness are presented.
- Chapter 3 is concerned with the short-term effectiveness of Graded Exercise Therapy in patients with chronic shoulder complaints in primary care.
- Chapter 4 is concerned with the long-term effectiveness of Graded Exercise Therapy in patients with chronic shoulder complaints in primary care.
- Chapter 5 addresses the cost-effectiveness of Graded Exercise Therapy in patients with chronic shoulder complaints in primary care.
- Chapter 6 presents an evaluation of the intervention process and discusses the extent to which the programme is being applied according to protocol, the feasibility of the programme for patients with chronic shoulder complaints in a primary setting and the needs to improve the programme to facilitate implementation.
- Chapter 7 discusses the influence of the two recruitment strategies used on the outcomes in this trial.

The general discussion (Chapter 8) reviews the main results of the studies presented in this thesis, focussing on practical and methodological issues, and considers implications for clinical practice and future research.

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CHAPTER 2

Concepts, development, and study design

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ABSTRACT AND KEY WORDS

This paper discusses the rationale for and content of a newly developed treatment for shoulder complaints (SC) and the design of a randomised study, which is currently being conducted to test its effectiveness.

Background: In current practice, approximately 50% of all patients with SC mention limitations in the performance of daily activities and persisting pain after six months. To improve the functional ability of patients with chronic SC, despite their pain, we developed an operant behavioural and time-contingent Graded Exercise Therapy (GET) programme for use in a primary care setting. We present the theory and conceptual model underlying this programme, report on its development and content and describe the design of a randomised clinical trial to evaluate the programme's effectiveness and cost-effectiveness.

Methods: One hundred and thirty-two patients who suffer from SC for at least 3 months are being recruited in general practice. After inclusion in the study, patients are randomly allocated to the GET programme or to usual care.

Measures: Questionnaires will be used to measure factors like severity of the main complaint, functional limitations of daily activities, perceived recovery, global health status, shoulder pain, generic health-related quality of life and costs, assessed at baseline, during treatment (6 weeks) and after treatment (12, 26 and 52 weeks).

Key words: Shoulder complaints, behavioural therapy, randomised clinical trial, study design.

INTRODUCTION

Shoulder complaints (SC) are a very common problem in Dutch primary health care. The community-based one-year prevalence of chronic shoulder pain lasting more than three months has been estimated at 15% in 1998 (Picavet et al 2000). The annual incidence of SC registered in general practices in the Netherlands has been reported to be as much as 25 per 1000 patients (Sobel et al 1996). Approximately 50% of all patients who visit their general practitioner with a new episode endure complaints for up to six months and up to 40% report complaints after 12 months (Windt et al 1996). Musculoskeletal disorders, of which SC constitute the second largest group after low back disorders, account for the second largest share in healthcare costs (Meerding et al 1998).

To date, there is insufficient information on the aetiology, diagnosis, and prognosis of SC. Biological, psychological and social factors are generally assumed to be involved and to interact in the course of non-specific musculoskeletal pain (Engel 1980, Nielson and Weir 2001, Vlaeyen and Linton 2000). A clear model about pain as a result of interaction between nociceptive stimulation, pain perception, pain experience and pain behaviour has been described by Loeser (Loeser 1980). It is unclear, however, whether and to what extent biological, psychological, and social factors have a causal relation with the initiation of SC or with the transition from acute to chronic SC (van der Heijden 1999). It can be hypothesized, however, that these factors play a role in the course of SC, comparable to other non-specific musculoskeletal pain disorders (Linton 1995).

Over the last decades, cognitive and behavioural principles have been integrated into pain management and have proven to be effective (Guzmán et al 2001, Linton 1999, Morley et al 1999, Tulder et al 2001, Vlaeyen and Linton 2000). The focus is primarily on pain behaviour, fear-avoidance beliefs and the associated disability. Performance and conditioning of physical activities are important features from a behavioural point of view. Most studies on the effectiveness of cognitive behavioural therapy for musculoskeletal pain have been administered for chronic complaints in multidisciplinary settings (Morley et al 1999).

Given the high prevalence of SC and the tendency for these complaints to become chronic, we have developed a Graded Exercise Therapy (GET) programme for the primary care setting. This programme, which is administered by physiotherapists, is based on behavioural treatment principles. The programme aims to improve functional abilities in patients with SC, largely excluding pain as a primary target. This paper presents the theory and conceptual model underlying this programme, then discusses the development and content of this programme and finally describes the design of a study we are currently undertaking to evaluate its effectiveness and cost-effectiveness.

Several considerations induced us to publish separate articles on the design of the study and the results. The first is that this allows reflection on the study protocol as such, independently of the study results. Secondly, it allows us to identify protocol deviations that might influence study results. Thirdly, it allows publication bias to be avoided.

CONCEPTS OF THE GET PROGRAMME

Biomedical approach

Traditionally, the management of SC has been based on a disease-oriented biomedical model (Cyriax 1981, Uhthoff and Sarkar 1990). This model is based on a one-dimensional causal relationship between tissue pathology and signs of SC, which assumes that pain and disability

are caused by acute or chronic injury of articular or periarticular soft tissues of the shoulder. Biomedical treatments mainly focus on pain relief and the treatment of disability. There is limited evidence that biomedical based interventions speed up recovery in the short term for patients with SC, and long-term effects have been rather disappointing (Green 2003, van der Heijden 1999, Kroese 2002).

Biopsychosocial approach

Melzack and Wall's gate-control theory of pain has led to a broad discussion and new views on pain (Melzack and Wall 1965). Initially, (chronic) pain was considered to be a result of straightforward somato-sensory stimulation. Nowadays, there is general agreement that pain has sensory, affective and cognitive dimensions. The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" indicating that pain experience is subjective (Merskey and Bogduk 1994).

This reconceptualization of pain had led to the development of a new multidimensional biopsychosocial model in which biological, psychological, and social factors contribute to produce pain experience and its persistence (Fordyce 1976, Nielson and Weir 2001, Turk and Okifuji 1997).

Operant conditioning approach

A behaviourally oriented operant conditioning approach focuses on environmental reinforcement contingencies of pain behaviour and pain-related inactivity in the maintenance of pain. According to learning theory principles, pain behaviour is acquired and can be modified through new learning experiences (Skinner 1953). Pain behaviour is considered to be conditional on the consequences of this behaviour. Positive or negative reinforcement may provoke continuation of the performed pain behaviour.

Fordyce et al first described the theoretical concept of operant behavioural treatments (Fordyce 1976). Characteristics of these treatments are reinforcement, rewarding, target setting and activity scheduling. To date, the effectiveness of operant behavioural treatment programmes has been documented in several studies (Morley et al 1999). Moreover, graded activity programmes have been shown to improve the level of daily activities and reduce disability in patients with subacute back pain (Fordyce et al 1986, Lindstrom et al 1992) and those with chronic back pain (Turner and Clancy 1988).

DEVELOPMENT OF THE GET PROGRAMME

The GET programme has been developed by experts in the field of operant behavioural treatments for chronic pain, together with a steering committee of primary care physiotherapists. Important in the area of behaviour change is to increase levels of daily activity including goal setting, pacing of progress towards goals, and manipulation of cues for and consequences of behaviours to promote change. The main elements of the GET programme are graded activity, time contingency, and operant conditioning (Fordyce et al 1986, Turk and Okifuji 1999).

Graded activity

In graded activity, levels of activity increase in a step-wise fashion. Graded activity has biomedical and psychosocial aims: improving functional ability, shifting attention from pain

to activity and provoking healthy behaviour. Behavioural activation is assumed to improve functional ability in patients with chronic musculoskeletal pain (Fordyce 1986).

Time-contingency

Whereas a disease-oriented pain-contingent approach involves activities that are performed and adjusted according to pain experience, a time-contingent approach involves levels of activity that are structured in time. The intensity of exercises rises gradually over time, irrespective of pain experience, with fixed quota agreed upon at the start of the programme.

Operant conditioning

By changing the consequences of behaviour, operant learning principles are used to promote and improve healthy behaviour. Positive reinforcement of the preferred behavioural changes is given to increase and maintain the frequency of graded activities.

External reinforcement is related to social and environmental factors. Reinforcement on healthy behaviour is given directly by the physiotherapist who acts like a coach. Initially, the emphasis is on external positive reinforcement to provoke behavioural changes. When behaviour has changed in the preferred direction, external reinforcement becomes less intensive and internal reinforcement becomes more important for the maintenance of the healthy behaviour. Internal reinforcement depends on the benefits patients experience as a consequence of healthy behaviour. Patients will become more motivated if they succeed in the performance of preferred activities and experience the progress made as a consequence of their own healthy behaviour.

CHARACTERISTICS OF THE GET PROGRAMME

The primary aim of this exercise programme is the patients' ability to perform their own preferred shoulder activities in daily life at home or at work, irrespective of the pain experience. It does not aim to achieve pain relief at all. The programme's activities are related to specific shoulder functions such as reaching, supporting, pushing, pulling, hitting, and stabilizing, with work-related activities receiving special attention.

A total of 18 one hour sessions are held over a period of 12 weeks. The programme is administered in small groups of three to five persons under the supervision of a specially trained physiotherapist. Since not all participants do have to start the programme at the same time, some patients in the group may already have made some progress in their rehabilitation plan while others have just joined the group.

Content of the GET programme

The programme consists of a start-up period and a treatment plus generalization period.

Start-up period

The programme starts with history taking, physical examination, and identification and assessment of the patient's own preferred activities. Special attention is paid to patients' experiences, beliefs, and behaviour with respect to the complaints and to possible barriers and obstacles towards recovery and increasing activity levels. At this stage, reconceptualization of pain and pain-related disability is important to ensure that patients are convinced they are able to control and influence their pain experience (Turk and Okifuji 1999). The treatment rationale is explained and aims of the treatment programme are set in terms of functional goals.

During the start-up period, which lasts two weeks, patients are asked to perform and adjust their own preferred activities on the basis of pain-contingency, the assumption being that levels of activity will be high if pain levels are low and vice versa. Levels of activity are registered in graphs that are used to evaluate progress as a consequence of the patients' actual behaviour.

At the end of the start-up period, the baseline for treatment is determined. Because the experience of pain is assumed to lead to limited progress, the level of activity at the start of the treatment period is set slightly below the average of the patient's pain-contingent performance, making it likely that the patient can complete the activities successfully. Positive experiences as a consequence of their initial treatment activities are expected to motivate patients to proceed with further exercises.

Goals, quota, and the precise content of the treatment period are determined and agreed upon for every individual patient. Goals are related to the patient's own preferred daily activities. The patient signs a contract setting out the patient-tailored rehabilitation plan, which defines quota for the treatment period by means of grading, that is, goal setting and time scheduling (figure 1).

Figure 1. Graded Exercise Therapy programme

Note

During the start-up period, levels of activity are adjusted by pain perception (pain-contingent). During the treatment period, levels of activity are based on pre-set quota in time (time-contingent), starting slightly below the level at baseline and increasing in a stepwise fashion to achieve pre-set goals at the end of the programme.

Treatment plus generalization period

The second phase, lasting 10 weeks, involves graded activity exercises. Activities are now structured according to a time-contingent approach, and the intensity of the exercises is gradually increased over time.

At the start of the treatment period, positive reinforcement of healthy behaviour is emphasized. Gradually, reinforcement becomes intermittent and less intense, while graphs are used as an instrument to reinforce patient behaviour and to discuss and evaluate the steps that have been achieved. Progress is attributed to the patient's performance.

Special attention is paid to the application of what has been learned in everyday life, that is, how to deal with new goals and how to manage a relapse or a new episode of complaints. This is called generalization. Generalization already starts at the beginning of the treatment period, but is strongly emphasized at the end of the treatment period.

DESIGN OF THE GET EVALUATION STUDY

Objectives

The GET trial is designed to study whether GET is a clinically effective and cost-effective treatment of patients with chronic SC after 6 and 12 months (figure 2). GET is compared with usual care (UC) according to the guideline for SC issued by the Dutch College of General Practitioners (DCGP) 1999 version. The following research questions will be addressed in this study:

- 1 Is GET clinically more effective than UC on performance of daily activities, perceived recovery, global health status, shoulder pain, and generic health-related quality of life after 6 and 12 months in patients with chronic SC
- 2 Is GET more cost-effective than UC after 12 months in patients with chronic SC

Recruitment and allocation of patients

Thirty-two general practitioners (GPs) in the province of Limburg, the Netherlands, are currently recruiting patients who suffer from SC. The period of enrolment runs from January 2002 until July 2003. Patients who visit their GP and meet the selection criteria are asked to participate in the study. A research assistant visits potential participants at home within two weeks after they have visited the GP. Patients are eligible for inclusion if they are at least 18 years of age and have suffered from shoulder pain or complaints in the shaded area shown in figure 3 for at least three months.

Furthermore, patients have to suffer from SC at the time of intake. Exclusion criteria are: treatment for their SC during the three months prior to the initial GP consultation; complete rotator cuff tears; serious prior traumata, i.e. fractures or dislocations, or prior surgery of the shoulder, upper limb, neck or thorax; osteoporosis, rheumatoid or bacterial arthritis, a tumour, referred pain from internal organs, a cervical radicular syndrome, gross shoulder hypermobility, stroke, polyneuropathy, multiple sclerosis, polymyalgia or ankylosing spondylitis; treatment for serious psychiatric disorders or unable to complete questionnaires in Dutch.

Sample size

Sample size calculations are based on perceived recovery rates since rates of performance of daily activities are not available. Recent studies of shoulder treatment in general practice show that six months after the first consultation, about 50% of all patients report full recovery or that their complaints are much improved. Since only patients with complaints lasting at least three months participate in the study, we estimate that only 25% of these patients feel fully recovered or much improved at six months after randomisation. Since we

Figure 2. Flow-chart of study design

Figure 3. Area of shoulder complaints

aim at a 1-sided alpha of 5%, a statistical power (1-beta) of 0.90, and a 10% dropout rate, we need 66 persons per treatment group to increase the recovery rate from 25% to 50%. The number needed to treat is calculated to be four.

Informed consent and randomisation

After giving their informed consent to participate in the study, patients are randomised to receive either GET or UC. A random number list generated by a researcher who is not involved in the conduct of the study is used to allocate patients.

Intervention

GET

GET is protocolized and carried out as described above. At the start of the intervention, patients are given a short brochure about the rationale behind the therapy, as well as a booklet containing graphs to evaluate progress and a treatment agreement to promote compliance with the programme.

UC

Usual care is standardized according to the 1999 version of the guidelines for SC issued by the DCGP (Winters et al 1999) and consists of information, recommendations and medical or drug therapy. This usual care of SC is pain-contingent. The GP makes the specific choice of treatment.

Physiotherapists and general practitioners

Prior to the start of the study, physiotherapists participating in the GET group took part in a one-day workshop and two booster sessions under the supervision of experts in the field of cognitive-behavioural treatments (A.K. and R.P.). General practitioners participating in the UC group have been given a refresher course on using the 1999 guideline for SC of the DCGP.

Baseline and follow-up measurements

Patients are seen for collection of baseline data before randomisation, during the intervention at 6 and 12 weeks after randomisation, and after completion of the treatment at 26 and 52 weeks after randomisation. At all these moments, the variables shown in table 1 are assessed.

In addition, demographic variables, disease characteristics, co-morbidity, physical activity, workload and treatment credibility and preferences are documented at baseline. Function of the shoulder girdle and cervicothoracic spine, severity of the main complaint, and psychosocial variables (anxiety, depression, somatization, distress and job content) are regarded as prognostic variables.

Clinical effectiveness

Performance of daily activities as outcome variable of clinical effectiveness is measured by the severity of the main complaint and functional limitations of daily activities. Perceived recovery as outcome variable of clinical effectiveness is measured on a seven-point ordinal scale. Patients are regarded as recovered if they feel either fully recovered or much improved. Global health status, shoulder pain, and generic health-related quality of life are also assessed as outcome variables of clinical effectiveness. Process measures include kinesiphobia, fear avoidance beliefs and fear of re-injury, catastrophizing, coping with pain, and internal and external locus of control.

Table 1. Variables

Variable	Measure					
	T=0	T=1	T=2	T=3	T=4	
Baseline status						
Demographic variables	X					
Specific disease characteristics	X					
Co-morbidity	X					
Physical activity	X					
Workload	X					
Treatment credibility and preference	X					
Prognostic variables						
Function of shoulder girdle	X					Physical examination
Function of cervicothoracic spine	X					Physical examination
Severity of main complaint	X					8-dimension inventory
Psychosocial variables	X					4DSQ
Job content	X					
Outcome variables						
Performance of daily activities						
1 Severity of main complaint	X	X	X	X	X	11-point Likert scale
2 Functional limitations of daily activities	X	X	X	X	X	Shoulder Disability Questionnaire
Perceived recovery of complaints		X	X	X	X	8-point scale
Global health status		X	X	X	X	
Shoulder pain	X	X	X	X	X	Shoulder Pain Score
Quality of life	X	X	X	X	X	EQ5D
Costs			Continuous			Cost diary
Process variables						
Kinesiophobia	X	X	X	X	X	Tampa Scale for Kinesiophobia
Fear-avoidance beliefs	X	X	X	X	X	Fear-Avoidance Beliefs Questionnaire
Catastrophizing	X	X	X	X	X	Pain Coping and Cognition List
Coping with pain	X	X	X	X	X	Pain Coping and Cognition List
Internal locus of control	X	X	X	X	X	Pain Coping and Cognition List
External locus of control	X	X	X	X	X	Pain Coping and Cognition List

Notes:

T=0 (baseline), T=1 (6 weeks), T=2 (12 weeks), T=3 (26 weeks) and T=4 (52 weeks)

4DSQ Four Dimensions of psychological Symptomatology Questionnaire (Terluin 1998)

SDQ Shoulder Disability Questionnaire (van der Heijden et al 2000)

SPS Shoulder Pain Score (Winters et al 1996)

EQ5D Quality of life (Brooks 1996)

TSK-DV Tampa Scale for Kinesiophobia (Vlaeyen et al 1995)

FABQ-DV Fear-Avoidance Beliefs Questionnaire (Vendrig et al 1998)

PCCL Pain Coping and Cognition List (Berg et al 2001)

Cost-effectiveness

To evaluate the short-term and long-term cost-effectiveness of GET, the following socio-economic endpoints are collected: programme costs, direct health care costs, direct non-

medical costs and indirect costs. Costs are measured by means of patient cost diaries (Goossens et al 2000). The effects are measured in terms of generic health-related quality of life descriptions measured with the EQ5D (Brooks 1996).

Blinding

Two research assistants who are not involved in the randomisation procedure carry out the data collection of baseline characteristics, process- and outcome measurements. Blinding of patients and health care providers (e.g., physiotherapists and general practitioners) is not possible. Data entry, intention to treat analysis, and cost analysis will be carried out independently and blinded for treatment allocation.

Data presentation and statistical analysis

Baseline data, which are relevant for comparability of groups, will be presented. Dropouts and losses-to-follow up will be described.

Analyses will be performed on the primary outcome measures, i.e., severity of the main complaint and functional limitations of daily activities, and on other clinical outcome measures, i.e., perceived recovery, global health status, shoulder pain, and generic health-related quality of life. T or F tests will be used to compare groups for outcome variables measured on continuous scales and Gaussian data distribution, while Mann-Whitney tests will be used for non-Gaussian distributions and chi-square tests for ordinal and dichotomous outcome variables.

The primary endpoint, i.e. the change in performance of daily activities at 6 and 12 months will be compared using the average change over time of both groups. The difference between those averages and its 95% confidence interval will be calculated. Effect measurements, point estimates and 95% confidence intervals will be presented.

Baseline characteristics that a priori are considered to be possible prognostic factors for performance of daily activities, with post randomisation differences between the groups, will be handled as potential confounders. Their influence will be evaluated by means of multivariable regression analyses. In case of confounding, adjusted effect estimates will also be reported. In the analyses of the difference in change for the primary end point at 6 and 12 months we will account for the repeated measures character of the data.

All patients will primarily be analysed according to the intention-to-treat principle. In order to study the influence of protocol violations on the study outcomes, an on-treatment-analysis will be performed. Patients with documented deviations from the study protocol will be excluded from this on-treatment analysis.

Qualitative evaluation of content and feasibility

A qualitative evaluation of the trial progress is being performed concomitantly. Treatment reports and questionnaires completed by the patients allocated to GET and the physiotherapists involved are used to evaluate the content of GET at the end of each treatment period. Interviews with patients allocated to UC and their UC providers are used to evaluate the content of the control treatment.

Feasibility and applicability of the GET programme will be evaluated at the end of the study. Experiences with and beliefs about the content of the programme, among both patients and physiotherapists, will be evaluated in focus group discussions.

DISCUSSION

Since it is as yet unclear whether and which patients will benefit from the GET programme, we only exclude patients on the basis of systematic diseases, referred pain or severe biomedical or psychiatric disorders. We consider the programme most suitable for patients with discrepant pain behaviour and pain beliefs. They might either postpone activities because they believe activity may cause damage or re-injury, or ignore the pain and consequently exceed suitable levels of activity. We hope this study will contribute to further insights into the applicability of behavioural treatments in musculoskeletal pain.

The present study is characterized by randomised allocation, cost-effectiveness evaluation and qualitative process evaluation. However, since blinding patients is not possible in this pragmatic study, information bias has to be taken into account. GET's contribution towards total effects cannot be evaluated in absolute terms because the study does not have an add-on design. There is some uncertainty as to required sample size, because calculations are based on rates of recovery and not on rates of performance of daily activities.

Although the GET programme could be embedded in a multidisciplinary approach to SC, it was developed to be administered in a primary care physiotherapy setting. It is obvious that professional capacities and attitudes towards SC among health care providers are extremely important. Physiotherapists do have capacities in terms of coaching patients in their physical activities, but special training in the treatment of psychological factors of pain and disability appears to be necessary.

Approval

The design of the study presented here has been approved by iRv/SRL's nationally recognized Medical Ethics Committee.

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CHAPTER 3

Short-term effectiveness

Published as

Geraets JJXR, Goossens EJB, Groot IJM de, Bruijn CPC de, Bie RA de, Dinant GJ, Heijden GJMG van der, Heuvel WJA van den. Effectiveness of a graded exercise therapy programme for patients with chronic shoulder complaints. *Austr J Physiother.* 2005; 51: 87-94.

ABSTRACT

An operant behavioural and time-contingent Graded Exercise Therapy (GET) programme to improve functional ability irrespective of pain experience in patients with chronic shoulder complaints (SC) was developed. The clinical effectiveness of GET compared to usual care (UC) was evaluated in a randomized clinical trial.

Assessments were carried out before and after 12 weeks of treatment. Performance of daily activities was measured by two outcome measures: the main complaints instrument and the Shoulder Disability Questionnaire (SDQ). Patients were eligible for participation if they had suffered from SC for at least three months. Patients suffering from systemic diseases, referred pain or severe biomedical or psychiatric disorders were excluded.

Patients (N=176) were randomized and allocated either to GET (N=87) or UC (N=89). GET led to larger improvement in the performance of daily activities than UC. However, only mean differences between groups in performance of activities related to the main complaints reached statistical significance ($P=0.049$, 95% CI: 0.0, 15.0). The observed beneficial effects were considered to be small to moderate (calculated effect sizes: 0.30 for the main complaints instrument and 0.07 for the SDQ). Subgroup analysis showed larger improvements on the main complaints instrument in patients not reporting pain reduction over time. GET seems to be less effective in restoring performance of daily activities as assessed by the SDQ in patients showing a painful arc during physical examination.

Results showed that GET is more effective in restoring performance of daily activities in patients with chronic SC than UC, although beneficial effects are small.

Key words: Shoulder complaints, behavioral therapy, randomized clinical trial.

INTRODUCTION

Shoulder complaints (SC) are a major topic in primary health care: the 1998 point prevalence of self-reported shoulder pain in the general Dutch population was estimated at 21%, while 41% of all patients with SC in the past 12 months visited a general practitioner (GP) (Picavet and Schouten 2003). A majority of SC last for relatively long periods of time or recur: approximately 50% of all patients who visit their GP with a new episode endure complaints for up to 6 months (Kuipers et al 2004, Windt van der et al 1996, Winters et al 1997 and 1999) and up to 40% still have complaints after 12 months. Moreover, 46% of all patients with a new episode of complaints recall a previous history of SC (Windt van der et al 1996). Eighty-five percent of patients with initial chronic shoulder pain in the general Swedish population still reported pain after 12 years (Andersson 2004).

Patients with SC suffer from pain (27%) and disability (29%) (Heijden van der 1999, Picavet and Schouten 2003). Because SC can have considerable impact on daily life and often develop into a chronic disorder, it is important to optimize the treatment. It has been hypothesized that the course of SC involves biological, psychological, and social factors, as is also the case in other non-specific musculoskeletal pain disorders (Linton 1995). We therefore developed an operant behavioural and time-contingent Graded Exercise Therapy (GET) programme to improve functional ability in patients with chronic SC despite their pain. We chose this approach in view of the proven effectiveness of this type of treatment in patients with low back pain (Fordyce et al 1986, Guzmán et al 2001, Lindstrom et al 1992, Linton 1999, Morley et al 1999, Tulder et al 2001, Vlaeyen and Linton 2000). We have previously described the theory and conceptual model underlying this programme, reported on the programme's development and content, and presented the design of our study (Geraets et al 2004). The present paper describes the clinical effectiveness of GET in patients with chronic SC. GET is compared to usual care (UC) as described in the 1999 guidelines for SC issued by the Dutch College of General Practitioners (DCGP) (Winters et al 1999; see also <http://nhg.artsennet.nl/upload/104/guidelines2/E08.htm>). The objective of the study was to assess whether GET is more effective than UC after 12 weeks of treatment in terms of restoring the performance of daily activities irrespective of pain experience in patients with chronic SC.

METHODS

Design

The short-term clinical effectiveness of Graded Exercise Therapy (GET) compared to usual care (UC) was assessed in a randomized clinical trial. Short term was defined as the end of the 12-week treatment period. GET was administered by 20 physiotherapists (PTs), whereas UC was administered by 32 general practitioners (GPs). The study was approved by iRv/SRL's Medical Ethics Committee.

Recruitment and allocation of patients

Patients with chronic SC (lasting for at least three months) living in the Province of Limburg, the Netherlands, were invited to participate in the study in the period from January 2002 until July 2003. With 25% and 50 % recovered patients in respectively the usual care and GET group at 26 weeks follow-up, we aimed at 132 patients to participate in the study (66 in each intervention group) based on a 1-sided alpha of 0.05, a statistical power (1-beta) of 0.90, and

a 10% non-differential dropout rate. Patients were recruited either by the GPs during consultation for SC, or by advertisement in local newspapers. All potential participants received written information and visited the GP to check eligibility according to the criteria listed below. A research assistant visited the patients at home for the intake procedure, within two weeks after the consultation with the GP. Eligible patients were asked to give written informed consent. Patients were included if they were at least 18 years of age and had suffered from SC in the shaded area shown in figure 1 for at least three months.

Figure 1. Area of shoulder complaints

Exclusion criteria were: medical treatment for SC during the previous three months; complete rotator cuff tears; serious prior traumata, i.e., fractures or dislocations; prior surgery of the shoulder, upper limb, neck or thorax; osteoporosis; rheumatoid or bacterial arthritis; a tumour; referred pain from internal organs; a cervical radicular syndrome; gross shoulder hypermobility; stroke; polyneuropathy; multiple sclerosis; polymyalgia; ankylosing spondylitis; treatment for serious psychiatric disorders or inability to complete questionnaires in Dutch.

Randomization and allocation

Patients were pre-stratified at PT practice level. We used block randomization, with blocks of 10 patients, to allocate patients either to GET or to UC in each stratum. Concealed randomization was based on a random number list generated by an experienced researcher who was not involved in the conduct of the study. Patients received prepared opaque sealed and coded randomization envelopes after the baseline measurements.

Interventions

Graded Exercise Therapy

GET is a behavioural treatment programme characterized by graded activity, time contingency and operant conditioning. The primary aim of this exercise programme is to increase the patients' ability to perform their own preferred shoulder activities in daily life at home or at work, irrespective of the pain experience. It does not aim to achieve pain relief at all. The programme's activities are related to specific shoulder functions such as reaching, supporting, pushing, pulling, hitting, and stabilizing, with work-related activities receiving special attention.

The content of the GET programme has been described in detail elsewhere (Geraets et al 2004).

An important aim of GET is to increase levels of daily activity by learning from the consequences of behaviours, the so-called operant learning principle (Fordyce 1976, Skinner 1953). Pain behaviour is expected to be consolidated when patients experience the consequences of this behaviour as pleasant and to be extinguished when they experience the consequences as unpleasant. Positive reinforcement of the preferred behavioural changes is given to increase and maintain the desired behaviour. In graded activity, levels of activity increase in a step-wise time-contingent fashion, irrespective of pain experience. Goals are preset and agreed upon at the start of the programme. The GET programme consists of a maximum of 18 group sessions each lasting approximately 60 minutes, over a period of 12 weeks, administered in groups of three to five persons. During the 'start-up period', the rationale is explained, and pain and pain-related disability are discussed. The 'treatment plus generalization' period involves the performance of operant conditioning and time-contingent graded exercises. At the start of the programme, the frequency of sessions is three times a week, after which it gradually decreases to one session every two weeks. Generalization to everyday life is strongly emphasized at the end of this phase.

Prior to the start of the study, physiotherapists (PTs) participating in the GET group (two in each of the ten local practices) took part in a one-day workshop and two booster sessions under the supervision of experts in the field of cognitive-behavioural treatment.

Usual Care

Usual care was standardized according to the 1999 version of the guidelines for SC issued by the Dutch College of General Practitioners (DCGP)(Winters et al 1999). UC consisted of information, recommendations and pain-contingent medical or drug therapy. During the first two weeks following the initial GP consultation, a wait-and-see policy was followed. This policy was supplemented with analgesics or NSAIDs if the GP thought this was necessary. The patient was instructed to re-consult the GP if complaints continued for more than two weeks. The GPs made the specific choice of treatment, like corticosteroid injections or referral to a PT or orthopedic surgeon. GPs participating in the UC group attended a refresher course on the application of the guidelines.

Blinding

Two research assistants who were not involved in the randomization procedure carried out the data collection of baseline characteristics and outcome measurements. Blinding of patients and health care providers (PTs and GPs) was not possible. Data entry and statistical analysis were carried out according to a pre-specified analysis plan and blinded for treatment allocation.

Baseline and outcome assessment

At baseline demographic variables, disease characteristics, and treatment preferences were documented (Table 1). Before randomization and after 12 weeks of treatment continuous outcome variables were documented.

The primary outcome variable, the performance of the level of daily activities, was assessed using two different assessment instruments: the main complaints instrument (a measure for the performance of activities related to patient-specific complaints) and the Shoulder Disability Questionnaire (SDQ) (Heijden van der et al 2000). In the first instrument, patients selected at baseline three daily activities they regarded as most important in relation

to their SC, but not necessarily related specifically to pain. They rated their ability to perform these activities during the past week on an ordinal (11-point) scale at baseline and during follow-up. The second instrument, the SDQ, is a functional status measure consisting of 16 statements regarding pain and limitations while performing common daily activities during the past 24 hours.

The secondary outcome measures we assessed were perceived recovery, shoulder pain, generic health-related quality of life, catastrophizing, coping with pain, kinesiophobia and fear-avoidance beliefs. Perceived recovery was measured on an eight-point ordinal scale (0 fully recovered – 7 very much deteriorated). Patients were regarded as recovered if they felt either fully recovered (0) or very much improved (1). Shoulder pain was scored on the Shoulder Pain Score (SPS) and pain intensity was measured on an 11-point ordinal scale (Winters et al 1996). Generic health-related quality of life was rated on the EQ5D (Brooks 1996). Catastrophizing and coping with pain were scored on subscales of the Pain Coping and Cognition List (PCCL) (Berg et al 2001). Kinesiophobia was assessed by two items (items 1 and 9) of the Tampa Scale for Kinesiophobia (TSK-DV) (Vlaeyen et al 1995). Fear-avoidance beliefs were scored on the subscale of fear-avoidance beliefs about physical activity, adjusted for SC, of the Fear-Avoidance Beliefs Questionnaire (FABQ-DV) (Vendrig et al 1998).

Statistical analyses

All data were analysed according to the intention-to-treat principle. Analyses were carried out with SPSS statistical software (11.5 version). A p-value of <0.05 was considered to be statistically significant (two-tailed) for all comparisons.

The primary endpoints, i.e., the change in the performance of daily activities at 12 weeks as assessed by the main complaints instrument and the SDQ, were compared using the average change over time in both groups. For all cases, we calculated the highest score of three selected main complaints at baseline and differences at follow-up. If two or three of the main complaints were rated equally high at baseline, we calculated mean differences over time.

Differences between groups were calculated and analysed by means of Student's T-tests for all outcome variables measured on continuous scales and having a Gaussian data distribution, and by Mann-Whitney tests for non-Gaussian distributions. Average change for groups, mean differences between groups, and 95% confidence intervals of the differences were calculated. Chi-square tests were performed for ordinal and dichotomous outcome variables. Risk differences were calculated and presented for dichotomous outcome measures. Effect-sizes were calculated by taking the mean differences between groups and dividing it by the standard deviation of the average change of the total population. We considered effect-sizes of 0.2, 0.5, and 0.8 as small, medium and large beneficial effects respectively (Cohen 1977).

We used imputation of the overall mean for missing data if patients of whom data were missing and patients eligible for analyses were comparable at baseline, that is if all baseline means of missing cases were no more than half of a standard deviation away from the overall means for continuous outcome measures and no more than 5 percent for dichotomous outcome measures.

We considered the following variables as putative prognostic factors: function of the shoulder girdle as assessed by physical examination (passive range of external rotation, active range of abduction/elevation, and presence of painful arc), psychosocial variables (anxiety, depression, somatization, distress) (Four Dimensions of psychological Symptomatology Questionnaire (4DSQ)) (Terluin 1998), and treatment preferences. Using a stepwise forward

procedure ($p < 0.10$) and the main complaint instrument and SDQ as outcome measures, the influence of these putative prognostic factors and post randomization differences between groups was evaluated by means of multiple linear regression analyses.

A change in shoulder pain intensity was considered a priori to be a modifier. We assumed that pain reduction over time might naturally result in increased performance of daily activities. Since the aim of GET is to increase performance of daily activities, irrespective of pain experience, we assumed that the programme might be more effective in patients not reporting pain reduction over time. Therefore, the influence of changes in pain intensity on performance of daily activities as a modifying factor was analysed. We defined subgroups based on pain reduction by more than one standard deviation away from baseline. We studied the effect of GET in these subgroups using multivariate linear regression for the main complaint instrument and for the SDQ. We also evaluated the interaction with treatment. Crude and adjusted regression coefficients and 95% confidence intervals are presented.

RESULTS

The GPs regarded 192 patients as eligible to participate in the study. Sixteen patients were excluded before randomisation (for reasons see figure 2), so 176 patients were randomized and allocated to either Graded Exercise Therapy (GET) ($N=87$) or usual care (UC) ($N=89$) (figure 2). Eighteen patients withdrew from the study during the treatment period. Six withdrawals had been allocated to GET (for reasons see figure 2), while 12 had been allocated to UC (for reasons see figure 2). Data for eight patients were missing at 12 weeks (2 GET and 6 UC).

Table 1 shows that at baseline, treatment groups were comparable on all continuous outcome measures. Patterns of treatment preferences were similar for both groups, although patients allocated to UC more frequently favored behavioural therapy and less frequently favoured manual therapy and drugs therapy (analgesics and NSAIDs). Patients allocated to UC scored slightly lower on the distress subscale of the 4DSQ and reported less frequent concomitant neck problems as well as more often a quick onset of their current complaints. Otherwise, prognostic status at baseline was comparable for both groups.

Patients who withdrew from the study during the treatment period ($N=18$) or had missing data at 12 weeks ($N=8$) were more likely to report a quick onset and a shorter duration of complaints, and had fewer prior episodes of SC during the past year. In terms of treatment preferences, they less frequently favored manual therapy and more frequently favoured drug therapy and injection therapy. Patients who withdrew scored slightly higher on the somatization subscale of the 4DSQ. No difference on the baseline values of outcome measures was found.

Table 2 shows that patients allocated to GET improved more than patients allocated to UC as measured on both primary outcome measures. Differences between groups for improvement of the main complaints reached statistical significance ($p=0.049$). Effect sizes for the main complaints instrument and the SDQ were calculated to be 0.30 and 0.07 respectively. Improvements on all secondary outcome measures favor GET, but only differences between groups for improvement of catastrophizing thoughts, reached statistical significance. Imputation did not alter these results.

Crude and adjusted analyses are presented in table 3. The between group difference for reduction of severity of the main complaint at 12 weeks post randomisation for patients receiving GET, was on average 7.5 points larger and statistically significant than for those

Figure 2. Flow-chart

receiving UC (model 1.1). The between group difference for reduction in SDQ score at 12 weeks post randomisation, favored GET, but failed to reach statistical significance (model 2.1).

Pain intensity was unchanged in 132 patients, while pain reduction was seen in 44 patients. There was a significant relationship between reduction of the severity of the main complaint at 12 weeks on the one hand and pain reduction and depression scores at baseline on the other hand (model 1.2). After adjustments for pain reduction and depression score at baseline, the difference in reduction of severity of the main complaint between treatment groups was retained at the conventional level (7.5 versus 7.6). When analyzed according to strata, mean differences between treatment groups for reduction of severity of the main complaint were larger in patients reporting no change in pain over time (7.6) than in patient reporting pain reduction (1.6).

Table 1. Baseline characteristics

	GET	UC	Eligible for analysis	Missing
Number	87	89	150	26
Demographic variables				
Age (years) (sd)	51.2 (13.2)	53.3 (11.7)	53.1 (12.6)	47.4 (10.3)
Female (%)	51	58	54	58
Specific disease variables				
<i>Present episode of SC:</i>				
Duration of shoulder pain (> 6 months) (%)	79	77	79	73
Sick leave (if paid employment) in past 8 weeks (> 1 week) (%)	4	12	7	13
Quick onset (%)	17	27	21	31
Concomitant neck problems (%)	54	40	47	50
<i>Cause of complaints</i>				
• Sudden movement (%)	6	7	6	8
• Overuse (%)	25	26	25	27
• Slight trauma (%)	3	5	3	9
• Others (%)	12	12	13	8
• Unknown (%)	40	35	37	39
<i>Prior episodes of SC:</i>				
Episodes of at least 1 week in past year (>5) (%)	68	69	70	61
Treatment preferences (no, unclear, yes) (%):				
• Behavioural therapy	6 / 88 / 6	12 / 73 / 15	9 / 81 / 10	12 / 80 / 8
• Physiotherapy	6 / 38 / 56	15 / 34 / 51	11 / 36 / 53	8 / 35 / 57
• Manual Therapy	7 / 80 / 13	21 / 59 / 20	12 / 70 / 18	25 / 63 / 12
• Analgesics	67 / 29 / 4	79 / 14 / 7	76 / 19 / 5	56 / 32 / 12
• NSAIDS	57 / 36 / 7	74 / 20 / 6	69 / 25 / 6	46 / 42 / 12
• Corticosteroid injection	71 / 26 / 3	75 / 21 / 3	76 / 21 / 3	58 / 38 / 4
• Surgery	76 / 22 / 2	84 / 14 / 2	81 / 17 / 2	73 / 23 / 4
Prognostic variables				
<i>Function of shoulder girdle</i>				
• Passive range of motion exorotation (<600) (%)	38	36	33	37
• Active range of motion abduction/elevation (<1500) (%)	17	15	17	24
• Presence of painful arc (%)	74	72	76	70
<i>Psychosocial (4DSQ) (%)</i>				
• Distress (medium/high) ¹	32	18	26	19
• Anxiety (medium/high) ²	2	4	4	0
• Depression (medium/high) ³	10	9	10	8
• Somatisation (medium/high) ⁴	43	33	34	54
Outcome variables Mean (sd)				
<i>Performance of daily activities:</i>				
• Severity of main complaints (0-100)	76.2(19.2)	71.9 (19.6)	74.3 (19.2)	72.3 (21.2)
• Functional limitations in daily activities (SDQ) (0-100)	66.0 (18.1)	65.6 (19.9)	65.7 (17.9)	66.3 (24.4)
Shoulder pain (SPS) (7-28)	17.9 (4.4)	17.1 (3.8)	17.4 (4.1)	17.8 (3.7)
Pain intensity (11-point scale) (0-10)	5.6 (2.2)	5.4 (1.8)	5.4(2.0)	6.3 (1.8)
Quality of life (EQ5D) (-1 to 1)	0.66(0.23)	0.69 (0.20)	0.68 (0.21)	0.64 (0.23)
Process variables Mean (sd)				
Kinesiophobia (2 items TSK) (1-7)	2.8 (1.9)	2.8 (2.0)	2.9 (1.9)	2.2 (1.8)
Fear-Avoidance Beliefs (5 items subscale FABQ) (1-7)	4.3 (1.3)	4.5 (1.3)	4.5 (1.3)	4.2 (1.4)
Catastrophizing (12 items subscale PCCL) (1-6)5	2.4 (0.8)	2.3 (0.8)	2.4 (0.8)	2.3 (0.9)
Coping with Pain (11 items subscale PCCL) (1-6)5	3.0 (1.0)	3.2 (0.9)	3.1 (0.9)	3.2 (0.9)
Internal locus of control (11 items subscale PCCL) (1-6)5	3.3 (0.9)	3.7 (0.8)	3.5 (0.9)	3.5 (0.8)
External locus of control (7 items subscale PCCL) (1-6)5	2.9 (0.8)	3.0 (0.8)	2.9 (0.9)	2.9 (0.8)

1 Distress: low (0-10), medium (11-20), high (21-32)

2 Anxiety: low (0-7), medium (8-12), high (13-24)

3 Depression: low (0-2), medium (3-5), high (6-12)

4 Somatisation: low (0-10), medium (11-20), high (21-32)

5 PCCL subscale scores: very low (1.0-1.9), low (2.0-3.4), high (3.5-5.0), very high (5.1-6.0)

Table 2. Mean improvement per outcome measure after 12 weeks of treatment¹

Primary outcome measures							
	GET	Usual Care	Differences between groups				
	N=87	N=89					
	Mean (sd)	Mean (sd)	Mean diff	95% CI of diff ²		P-value ³	Effect size
				lower	upper		
Main complaints (0-100)	32.8 (25.7)	25.3 (24.5)	7.5	0.0	15.0	0.049	0.30
SDQ (0-100)	17.0 (26.0)	15.3 (21.6)	1.7	-5.4	8.8	0.642	0.07
Secondary outcome measures							
Shoulder pain (7-28)	3.0 (3.3)	2.3 (3.4)	0.7	-0.3	1.7	0.165	0.21
Pain intensity (0-10)	1.7 (2.2)	1.5 (2.2)	0.3	-0.4	1.0	0.375	0.13
Quality of life (-1 to 1)	0.06 (0.22)	0.06 (0.18)	0.00	-0.06	0.06	0.929	0.00
Fear avoidance (1-7)	0.4 (1.4)	0.2 (1.0)	0.1	-0.2	0.5	0.449	0.12
Kinesiophobia (1-7)	0.2 (1.6)	0.0 (1.8)	0.2	-0.3	0.7	0.411	0.13
Catastrophizing (1-6)	0.4 (0.7)	0.2 (0.5)	0.2	0.0	0.4	0.028	0.33
Coping (1-6)	0.1 (0.8)	0.0 (0.7)	0.1	-0.2	0.3	0.499	0.11
	GET	Usual Care	Differences between groups				
	N (%)	N (%)	Risk Difference			Chi-square	P-value
Perceived recovery (yes/no)	23 (29.1)	13 (18.3)	0.11			0.122	

¹ After imputation of the overall mean² 95% confidence interval of difference³ Statistically significant $P < 0.05$

There was a significant relationship between reduction in SDQ scores at 12 weeks on the one hand and pain reduction and presence of a painful arc at baseline on the other hand (model 2.2), and in addition for the interaction between GET * Painful arc (model 2.3). After adjustment for pain reduction, for presence of painful arc at baseline, and for the interaction between GET * Painful arc, the difference in reduction of severity of disability (SDQ) between treatment groups changed substantially (from 1.7 to 10.8). When analysed according to strata, mean differences between treatment groups for reduction of severity disability (SDQ) were smaller and favored UC in patients with a painful arc (-0.2) as compared with patients with no painful arc (7.3). These findings suggest that in terms of improvement of the SDQ scores GET was less effective in patients showing a painful arc at baseline.

DISCUSSION

Our findings suggest that the operant behavioural Graded Exercise Therapy (GET) programme is more effective than usual care (UC) in restoring daily activities in patients with chronic shoulder complaints. However, only differences between groups for the main complaint instrument reached statistical significance and we consider the observed beneficial effects to be small. Performance of daily activities was measured by two outcome measures (main complaints instrument and SDQ). Patients allocated to GET improved more on both measures than those allocated to UC, although differences between the groups were only statistically significant for

Table 3. Crude and adjusted analysis of primary outcome measures¹

Variables		B ²	B ³	B ⁴	95% CI of difference		P-value
					lower	upper	
<i>Main complaints; mean differences between groups (0-100)</i>							
Model 1.1	GET (GET=1; UC = 0)	7.5			0.0	15.0	0.049
Model 1.2	GET (GET=1; UC = 0)		7.6		0.9	14.3	0.026
	Change in pain intensity (changed=1; unchanged= 0)		26.8		19.3	34.4	0.000
	Depression (medium/high=1; low= 0)		8.3		0.1	16.6	0.048
<i>SDQ; mean differences between groups (0-100)</i>							
Model 2.1	GET (GET=1; UC = 0)	1.7			-5.4	8.8	0.642
Model 2.2	GET (GET=1; UC = 0)		0.6		-5.6	6.9	0.840
	Change in pain intensity (changed=1; unchanged = 0)		23.6		16.3	30.8	0.000
	Painful arc (present=1; absent = 0)		-10.3		-17.4	-3.3	0.004
Model 2.3	GET (GET=1; UC = 0)			10.8	-1.2	22.7	0.077
	Change in pain intensity (changed=1; unchanged = 0)			24.6	17.3	31.8	0.000
	Painful arc (present=1; absent = 0)			-3.5	-13.3	6.3	0.486
	GET * Painful arc (GET=1; UC = 0) (present=1; absent = 0)			-14.0	-28.1	0.1	0.051

¹ After imputation of the overall mean² Regression coefficient model adjusted only for GET³ Regression coefficient model adjusted for depression and presence of painful arc at baseline and for change in pain intensity.⁴ Regression coefficient model adjusted for presence of painful arc at baseline, interaction between GET and presence of painful arc at baseline and for change in pain intensity.

changes in performance of activities related to patients' main complaints. The SDQ is an instrument to assess activities in terms of functional limitations related to pain. Given the aim of the GET programme, which is not primarily to reduce pain intensity, SDQ changes might be expected to be less obvious. Nevertheless, patients allocated to GET showed greater changes in shoulder pain than those allocated to UC. Shoulder pain reduction was considered a priori to be a modifying factor. Mean differences between groups as assessed by the main complaints instrument were higher in patients not reporting pain reduction. GET was more effective in restoring

performance of daily activities as assessed by the SDQ in patients not reporting a painful arc. For clinical practitioners like GPs and PTs, these results mean that GET seems to be particularly effective in improving the performance of daily activities among patients who eventually show little reduction of pain intensity. GET seems less effective in patients who report a painful arc during physical examination. However, since only 44 participants (26%) reported pain reduction post treatment, and since a painful arc was absent in only 48 patients (28%), these outcomes need to be interpreted with caution. We suggest that these factors should be evaluated in greater detail in further studies.

GET is a behavioural treatment and not a cognitive behavioural treatment. Nevertheless, data show that GET had positive effects on all psychological outcome measures. The positive effect on catastrophizing thoughts was even statistically significant ($p=0.028$).

Thirty-six patients (23 GET versus 13 UC) reported recovery post treatment (full recovery or very much improved). Differences between groups in perceived recovery rates were 11% and not statistically significant ($p=0.122$). But even though patients did not perceive themselves as recovered, performance of daily activities improved. These results implicate that patients allocated to GET consider their ability to perform daily activities at home or at work less frequently dependent of perceived recovery or pain experience.

As patients were only excluded from the trial on the basis of systemic diseases, referred pain or severe biomedical or psychiatric disorders, we regard our study population as fairly representative of persons with SC in the general practice population.

Treatment groups were comparable with respect to outcome measures at baseline. Blinding of patients and health care providers (PTs and GPs) for the nature of allocated treatment was not possible. However, although treatment preferences could therefore introduce bias these were found to have no influence on outcome measures after 12 weeks of treatment. Blinding could explain the differential rates for dropouts and loss to follow-up. Eighteen patients (10.2 %) withdrew from the study, and data for eight patients (4.5 %) were missing for post-treatment analysis. Although more withdrawals had been allocated to UC (12 UC versus 6 GET), the numbers of patients who withdrew because of the content of the interventions (frequency of treatment sessions and treatment preferences) were small and similar for both groups (3 UC versus 2 GET).

Since patients who withdrew from the study during treatment period ($N=18$) or had missing data at 12 weeks ($N=8$), had a shorter duration of complaints and had fewer prior episodes of SC during the past year, the prognostic status at baseline of these patients was probably slightly better compared to patients available for analysis (Windt van der et al 1996). Because the numbers of withdrawals per group were not equally balanced, we applied imputation of the overall mean for missing data. However, imputation of missing outcome data did not alter the results of this study.

This study confirms the hypothesis that behavioural factors play a role in the course of SC, which is comparable to that in other non-specific musculoskeletal pain disorders (Linton 1995, Vlaeyen and Linton 2000). Further evaluation of long-term effectiveness and cost-effectiveness is needed before implementation of GET can be recommended.

Our overall conclusion is that GET seems to be more effective than UC in restoring the performance of daily activities in patients with chronic SC, although beneficial effects are small. Mean improvements for the mean complaints instrument were larger in patients not reporting pain reduction. GET has a favourable effect on catastrophizing thoughts among patients with chronic SC. GET seems to be less effective in patients showing a painful arc during physical examination.

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CHAPTER 4

Long-term effectiveness

Submitted (revised version) as
Long-term effectiveness of a graded exercise therapy programme for patients with
chronic shoulder complaints. Geraets JJXR, Goossens MEJB, de Groot IJM, de Bruijn CPC,
de Bie RA, Dinant GJ, van den Heuvel WJA, van der Heijden GJMG.

ABSTRACT

Objective: The long-term effectiveness of a behavioural Graded Exercise Therapy (GET) programme in restoring performance of daily activities, compared with usual care (UC), in patients with chronic shoulder complaints in a primary care setting was assessed in a randomised clinical trial.

Methods: Primary outcome measures (main complaint, shoulder disability) and secondary outcome measures (perceived recovery, shoulder pain, generic health-related quality of life, catastrophising, coping with pain, internal locus of control, external locus of control, kinesophobia and fear-avoidance beliefs) were assessed before and directly after 12 weeks of treatment and during follow-up at 26 and 52 weeks.

Results: GET patients (N=87) showed statistically significantly greater improvement than UC patients (N=89) on the main complaint instrument directly after 12 weeks of treatment ($P=0.049$, 95% CI: 0.0, 15.0) and these improvements lasted for at least 52 weeks ($P=0.025$, 95% CI: 1.2, 17.3). GET was equally effective as UC in patients with a painful arc during physical examination and more effective in patients with no pain reduction during the treatment period. Significantly greater improvements with GET were found for catastrophising at 12 weeks ($P=0.028$, 95% CI: 0.0, 0.4) and for fear avoidance beliefs ($P=0.043$, 95% CI: 0.0, 0.8) and kinesophobia ($P=0.003$, 95% CI: 0.3, 1.3) at 52 weeks. Calculated effect sizes were rather modest (up to 0.45).

Conclusions: The effectiveness of GET compared with UC in restoring daily activities in patients with chronic SC, as assessed directly after treatment, persists in the long term (at least 52 weeks), although clinical benefits are rather modest.

Key words: Shoulder complaints, behavioural therapy, randomised clinical trial.

INTRODUCTION

Shoulder complaints (SC) have a tendency to last for prolonged periods of time or to recur (Luime et al 2004a). Earlier studies on the long-term course of SC in primary care in the Netherlands have shown that approximately 50% of all patients who visit their general practitioner (GP) with a new episode have complaints lasting up to 6 months (Windt van der et al 1996, Winters et al 1997, Kuipers et al 2004) and about 40% still have complaints after 12 months (Winters et al 1999a). Forty-six percent of all patients with a new episode of complaints recall a previous history of SC (Windt van der et al 1996). Recurrence rates for SC subsequent to complaints during the preceding year in a Dutch population of employed persons were estimated at 31% and 66% after 12 and 24 months respectively (Luime et al 2004b). Thus, chronic and recurrent SC are a major health problem. Nor is this problem unique to the Netherlands. Fifty-four percent of patients with SC in an open British population still reported shoulder pain after three years of follow-up (Macfarlane et al 1998) and 85% of patients with initial chronic shoulder pain in the general Swedish population still reported pain after 12 years (Andersson 2004).

Because SC can have considerable impact on daily life and often develop into a chronic disorder, it is important to optimise treatment in primary care. We hypothesised that – just as with other non-specific musculoskeletal pain disorders – biological, psychological and social factors would affect the course of SC (Linton 1995). The effectiveness of behavioural treatment in patients with chronic musculoskeletal pain has been documented in several studies (Fordyce et al 1986, Lindstrom et al 1992, Linton 1999, Morley et al 1999, Vlaeyen and Linton 2000, Guzmán et al 2001, Tulder et al 2001). However, most of these studies involved patients with chronic low back pain, and were conducted in secondary or multidisciplinary settings. There is limited evidence for operant-behavioural treatment (graded activity) on return to work and reduced sick-leave in low back pain patients (Staal et al 2004, Ostelo et al 2005, Jensen et al 2005). There is also limited evidence that there is no difference between behavioural treatments and exercise therapy in low back pain patients (Ostelo et al 2005). We have developed a behavioural Graded Exercise Therapy (GET) programme, to be administered by physiotherapists, which aims to improve functional ability and promote healthy behaviour and the long-term course in patients with chronic SC in a primary care setting. We have previously described the theory and conceptual model underlying this GET programme and presented the design of our study (Geraets et al 2004). We have also reported on the short-term clinical effectiveness of GET after 12 weeks of treatment (Geraets et al 2005): GET seemed to be more effective in restoring the performance of daily activities in patients with chronic SC after 12 weeks of treatment than usual care (UC). The question that remained was whether this favourable effect of GET would last. We therefore studied the long-term effectiveness of GET after 26 and 52 weeks in patients with chronic SC.

METHODS

Design

The objective of this randomised study was to see whether GET was more effective than UC in terms of restoring the performance of daily activities in patients with chronic SC in the long term (26 and 52 weeks after the start of the treatment). GET was administered by 20 physiotherapists (PTs), whereas UC was administered by 32 general practitioners (GPs). With

25% and 50% recovered patients in the usual care and GET groups, respectively, at 26 weeks follow-up, we would need 132 patients (66 in each intervention group) to reach statistical significance (2-sided alpha of 0.05, statistical power (1-beta) of 0.90, and 10% non-differential dropout rate). The study was approved by the iRv/SRL's Medical Ethics Committee.

Recruitment and allocation of patients

Patients who were at least 18 years of age, had suffered from SC for at least three months and were living in the Province of Limburg, the Netherlands, were invited to participate in the study between January 2002 and July 2003. Patients were recruited either by their GP during consultation for SC, or via advertisements in local papers. All potential participants received written information and consulted their GP, who checked their eligibility according to the criteria listed below. Within two weeks after the consultation with the GP, a research assistant visited the patients at home for intake and baseline assessment. Eligible patients were asked to give written informed consent.

Exclusion criteria were: medical treatment for SC during the previous three months; complete rotator cuff tears; serious prior traumata of the shoulder girdle, e.g. fractures or dislocations; prior surgery of the shoulder, upper limb, neck or thorax; osteoporosis; rheumatoid or bacterial arthritis; a tumour; referred pain from internal organs; a cervical radicular syndrome; gross shoulder hypermobility; stroke; polyneuropathy; multiple sclerosis; polymyalgia; ankylosing spondylitis; treatment for serious psychiatric disorders; and inability to complete questionnaires in Dutch.

Physiotherapists and general practitioners

Prior to the start of the study, physiotherapists (PTs) participating in the GET group (two in each of the 10 local practices) took part in a one-day workshop and two booster sessions under the supervision of experts in the field of cognitive-behavioural treatment. GPs participating in the UC group followed a refresher course on using the 1999 guidelines for SC of the Dutch College of General Practitioners (DCGP).

Randomisation and allocation

We used blocked randomisation, with blocks of 10 patients, to allocate patients either to GET or to UC. Concealed randomisation was based on a random number list generated by a researcher who was not involved in the conduct of the study. Patients received prepared opaque sealed and coded randomisation envelopes after the baseline measurements.

Interventions

Graded Exercise Therapy

GET is a behavioural treatment programme based on the principles of graded activity, operant conditioning and time-contingency. The programme attempts to improve the performance of daily activities, irrespective of pain experience, and to promote healthy behaviour e.g. to reduce utilisation of health care services and relevant non-health care services, in patients with chronic shoulder complaints. In graded activity, levels of activity increase in a step-wise time-contingent fashion. An important aim of GET is to increase levels of daily activity by learning from the consequences of pain behaviours, the so-called operant learning principles (Skinner 1953, Fordyce 1976). Pain and pain behaviour are assumed dependent on consequence-controlled learning. Pain behaviour is expected on the

one hand to consolidate when patients experience the consequences of this behaviour as pleasant and on the other hand to extinguish when they experience these as unpleasant. To promote and maintain the desired behaviour, PTs used graphs as an instrument to reinforce patient's behaviour and to discuss and evaluate the steps that have been achieved.

Table 1. Main elements of the Graded Exercise Therapy programme

Start-up period (approximately 6 sessions over a 2-week period)

- Rationale: Prior to the start of the programme, patients receive a short brochure explaining the rationale behind it.
- Reconceptualisation: Pain and pain-related disability are reviewed to ensure that patients are convinced they are able to control and influence their pain experience and improve levels of activity.
- Goal-setting: Treatment goals are set, related to the patient's own preferred daily activities.

Treatment plus generalisation period (approximately 12 sessions over a 10-week period)

- Graded Activity: Levels of activity are increased in a step-wise fashion.
- Time contingency: Levels of activity are structured in time and not according to pain experience.
- Operant conditioning: Environmental reinforcement is used to promote and improve healthy behaviour.
- Generalisation: What has been learned is applied to everyday life.

The main elements of the GET programme are listed in table 1. GET consists of a maximum of 18 group sessions of approximately 60 minutes over a period of 12 weeks, administered in small groups of three to five persons. At the start of the programme, the rationale is explained, pain and pain-related disability are discussed and goals are set and agreed upon. The 'treatment plus generalisation' period involves the performance of operant conditioning and time-contingent graded exercises. Initially, the frequency of sessions is fixed at three times a week, after which it gradually decreases to one session every two weeks. During the last phase of the treatment, generalisation to everyday life is strongly emphasised. The GET programme has been described in detail elsewhere (Geraets et al 2004).

Usual Care

Usual care was standardised according to the 1999 version of the guidelines for SC issued by the Dutch College of General Practitioners and consists of information, recommendations and pain-contingent medical or drug therapy (Winters et al 1999b; see also <http://nhg.artsennet.nl/upload/104/guidelines2/E08.htm>). During the first two weeks following the initial consultation with the GP, a wait-and-see policy is followed, supplemented with analgesics or NSAIDs if the GP thinks this necessary. Patients are instructed to re-consult their GP if complaints continue for more than two weeks. The GP makes the specific choice of treatment, like corticosteroid injections or referral to the PT or orthopaedic surgeon.

Blinding

Two research assistants who were not involved in the randomisation procedure collected data on baseline characteristics and outcome measurements. Patients and health care providers (PTs and GPs) could not be blinded. Data entry and statistical analysis were carried out according to a pre-specified analysis plan and blinded for treatment allocation.

Table 2. Baseline characteristics

Number	GET 87	Usual Care 89
Demographic variables		
Age (years) (sd)	51.2 (13.15)	53.3 (11.69)
Female (%)	50.6	58.4
Specific disease variables		
Present episode of SC:		
Duration of shoulder pain (> 6 months) (%)	79	77
Duration of limitation of daily activities in past year (> 1 month) (%)	15	24
Sick leave (if paid employment) in past 8 weeks (> 1 week) (%)	4	12
Quick onset (%)	17	27
Concomitant neck problems (%)	54	40
Cause of complaints		
• sudden movement (%)	6	7
• overuse (%)	25	26
• trauma (%)	3	5
• others (%)	12	12
• unknown (%)	40	35
Prior episodes of SC:		
• Episodes of at least 1 week in past year (>5) (%)	68	69
Treatment preferences (no, unclear, yes) (%):		
• Behavioural therapy	6 / 88 / 6	12 / 73 / 15
• Physiotherapy	6 / 38 / 56	15 / 34 / 51
• Manual Therapy	7 / 80 / 13	21 / 59 / 20
• Analgesics	67 / 29 / 4	79 / 14 / 7
• NSAIDs	57 / 36 / 7	74 / 20 / 6
• Corticosteroid injection	71 / 26 / 3	75 / 21 / 3
• Surgery	76 / 22 / 2	84 / 14 / 2
Prognostic variables		
Function of shoulder girdle		
• Passive range of motion exorotation (<600) (%)	38	36
• Active range of motion abduction/elevation (<1500) (%)	17	15
• Presence of painful arc (%)	74	72
Psychosocial (4DSQ) (%)		
• Distress (medium/high) ^a	32	18
• Anxiety (medium/high) ^b	2	4
• Depression (medium/high) ^c	10	9
• Somatisation (medium/high) ^d	43	33
Outcome variables Mean (sd)		
Performance of daily activities:		
• Severity of main complaints (0-100)	76.2 (19.18)	71.9 (19.6)
• Functional limitations in daily activities (SDQ) (0-100)	66.0 (18.06)	65.6 (19.86)
Shoulder pain (SPS) (7-28)	17.9 (4.43)	17.1 (3.77)
Pain intensity (11-point scale) (0-10)	5.6 (2.19)	5.4 (1.77)
Quality of life (EQ5D) (-1 to 1)	0.66 (0.234)	0.69 (0.198)
Process variables Mean (sd)		
Kinesiophobia (2 items TSK) (1-7)	2.8 (1.91)	2.8 (1.95)
Fear-Avoidance Beliefs (5 items subscale FABQ) (1-7)	4.3 (1.25)	4.5 (1.32)
Catastrophising (12 items subscale PCCL) (1-6) ^e	2.4 (0.84)	2.3 (0.79)
Coping with Pain (11 items subscale PCCL) (1-6) ^e	3.0 (0.96)	3.2 (0.89)
Internal locus of control (11 items subscale PCCL) (1-6) ^e	3.3 (0.94)	3.7 (0.83)
External locus of control (7 items subscale PCCL) (1-6) ^e	2.9 (0.84)	3.0 (0.84)

^a Distress: low (0-10), medium (11-20), high (21-32)^b Anxiety: low (0-7), medium (8-12), high (13-24)^c Depression: low (0-2), medium (3-5), high (6-12)^d Somatisation: low (0-10), medium (11-20), high (21-32)^e PCCL subscale scores: very low (1.0-1.9), low (2.0-3.4), high (3.5-5.0), very high (5.1-6.0)

Baseline and outcome assessment

Demographic variables, disease characteristics and treatment preferences were recorded at baseline (Table 2). Continuous outcome variables were recorded before randomisation; after 12 weeks of treatment and at 26 and 52 weeks of follow-up.

The primary outcome variable, i.e. the level of daily activities, was assessed using 2 different instruments: the 'main complaints' instrument, which is a clinically relevant and responsive measure for the performance of activities related to patient-specific complaints, and the Shoulder Disability Questionnaire (SDQ), which is a disease specific measure considered reliable and responsive (Beurskens et al 1999, Windt van der et al 1998, Heijden van der et al 2000). In the 'main complaints' instrument, patients selected at baseline the three most important daily activities that were affected by their SC, which were not necessarily related specifically to pain. They rated their ability to perform these activities during the past week on an ordinal (eleven-point) scale at baseline and during follow-up. The SDQ is a functional status measure consisting of 16 dichotomous items on pain and limitations experienced while performing daily activities during the past 24 hours (e.g. My shoulder is painful when I lie on it).

Secondary outcome measures were perceived recovery, shoulder pain, generic health-related quality of life, catastrophising, coping with pain, internal locus of control, external locus of control, kinesiophobia and fear-avoidance beliefs. Perceived recovery was measured on an eight-point ordinal scale (0 = fully recovered; 7 = very much deteriorated). Patients were regarded as recovered if they felt either fully recovered (0) or very much improved (1). Shoulder pain was scored on the Shoulder Pain Score list (SPS) which is considered valid and pain intensity was measured on an eleven-point ordinal scale (Winters et al 1996). Generic health-related quality of life was rated on the EQ5D which appeared to be sufficiently valid, reliable and responsive to change (Brooks 1996, Hurst et al 1997). Catastrophising, coping with pain, internal locus of control and external locus of control were scored on subscales of the Pain Coping and Cognition List reported to be sufficiently valid and reliable (PCCL) (Berg et al 2001). Kinesiophobia was assessed by two items (items 1 and 9) of the Tampa Scale for Kinesiophobia (TSK-DV) (Vlaeyen et al 1995). Fear-avoidance beliefs were scored on the subscale of fear-avoidance beliefs about physical activity of the Fear-Avoidance Beliefs Questionnaire (FABQ-DV), adjusted for SC (Vendrig et al 1998). The test-retest reproducibility and internal consistency of the FABQ have appeared to be satisfactory (Waddell et al 1993).

Furthermore, utilisation of direct health care services and relevant non-health care services during the 52 weeks follow-up period (GET and UC during the 12 weeks treatment period excluded) was documented. Utilisation of direct health care services included the number of visits to general practitioners, physiotherapists, manual therapists, Cesar/Mensendieck exercise therapists, physicians and/or alternative therapists and the number of prescriptions for medication after the treatment period. Utilisation of non-health care services included the number of hours of professional home care, of paid housekeeping, and of unpaid help from relatives or friends and the number of expenses for health-related activities (e.g. fitness training) and other out-of-pocket expenses (e.g. non-prescribed medication).

Statistical analyses

Data were analysed with SPSS statistical software, version 12.0.1 (SPSS, Inc. Houston, Texas), according to the intention-to-treat principle. A p-value of <0.05 was considered to be statistically significant (two-tailed) for all comparisons.

The primary endpoints, i.e., change in the performance of daily activities at 12, 26 and 52 weeks as assessed by the main complaint and the SDQ, were compared using the mean change over time in both groups. For all cases, we calculated the highest score of the three selected main complaints at baseline and the differences between baseline and follow-up. If two or three main complaints had been rated equally high at baseline we calculated mean differences over time.

Differences between groups were calculated and analysed by means of Student's t-tests for all outcome variables measured on continuous scales and having a Gaussian data distribution, and by Mann-Whitney tests for non-Gaussian distributions. Average change for groups, mean differences between groups and 95% confidence intervals of the differences were calculated. Chi-square tests were used for ordinal and dichotomous outcome variables. Risk differences and 95% confidence intervals were calculated and presented for dichotomous outcome measures. Effect sizes were calculated by taking the mean differences between groups and dividing them by the standard deviation of the average change for the total population. We regarded effect sizes of 0.2, 0.5 and 0.8 as small, medium and large beneficial effects, respectively (Cohen 1977).

We used unconditional imputation of the overall mean for missing data if patients whose data were missing and patients eligible for analysis were comparable at baseline, that is, if differences were no more than half of a standard deviation removed from the overall means for continuous outcome measures and no more than 5 percent for dichotomous outcome measures.

We regarded the following variables as putative prognostic factors: function of the shoulder girdle as assessed by physical examination (passive range of external rotation, active range of abduction/elevation and presence of painful arc), psychosocial variables (anxiety, depression, somatisation, and distress, assessed by the Four Dimensions of psychological Symptomatology Questionnaire (4DSQ)) (Terluin 1998), treatment preferences and recruitment strategy (either by GP or by advertisement). Using a stepwise forward procedure ($p < 0.10$) and taking the main complaint and SDQ as the outcome measures, we evaluated the influence of these putative prognostic factors and post-randomisation differences between groups by means of multiple linear regression analyses.

A change in shoulder pain intensity was considered a priori to be a modifying factor. We assumed that pain reduction over time might result in improved performance of daily activities as a natural course. Since the aim of GET is to improve the performance of daily activities, irrespective of pain experience, we considered the possibility that the programme might be more effective in patients without pain reduction over time. Therefore, the influence of changes in pain intensity on the performance of daily activities was explored and analysed as a modifying factor. We defined subgroups on the basis of pain reduction by more than one standard deviation of the overall mean of the pain intensity at baseline, and studied the effect of GET in these subgroups using multivariate linear regression for the main complaint instrument and for the SDQ.

RESULTS

The flow-chart of the recruitment process is presented in figure 1. The GPs regarded 192 patients as eligible to participate in the study. Sixteen patients were excluded before randomisation (for reasons see figure 1), 176 patients were randomised and allocated to either Graded Exercise Therapy (GET) ($N=87$) or usual care (UC) ($N=89$). Eighteen patients

Figure 1. Flow-chart

Table 3. Mean improvement on primary outcome measures after 12, 26 and 52 weeks^a
Overall and subgroup analyses

		GET N=87	Usual Care N=89	Differences between groups				
		Mean (sd)	Mean (sd)	Mean diff	95% CI of diff ^b		P-value ^c	Effect size
					lower	upper		
Main complaints (0-100)								
Overall analyses (GET-UC)								
12 weeks	N= 176 (87-89)	32.8 (25.7)	25.3 (24.5)	7.5	0.0	15.0	0.049	0.30
26 weeks	N= 176 (87-89)	38.4 (26.7)	31.2 (28.0)	7.1	-1.0	15.3	0.086	0.26
52 weeks	N= 176 (87-89)	41.1 (26.7)	31.8 (27.4)	9.2	1.2	17.3	0.025	0.34
Pain intensity reduced								
12 weeks	N= 44 (24-20)	50.7 (23.5)	49.1 (24.7)	1.6	-13.1	16.3	0.826	0.06
26 weeks	N= 110 (54-56)	49.1 (24.3)	43.1 (24.4)	6.0	-3.2	15.2	0.202	0.25
52 weeks	N= 114 (58-56)	49.9 (23.9)	43.3 (24.2)	6.6	-2.3	15.5	0.147	0.27
Pain intensity unchanged								
12 weeks	N= 132 (63-69)	25.9 (23.1)	18.4 (19.8)	7.6	0.2	15.0	0.045	0.35
26 weeks	N= 66 (33-33)	20.8 (20.8)	11.1 (21.8)	9.8	-0.7	20.2	0.068	0.46
52 weeks	N= 62 (29-33)	23.5 (23.3)	12.4 (21.1)	11.1	-0.2	22.4	0.054	0.50
SDQ (0-100)								
Overall analyses								
12 weeks	N= 176 (87-89)	17.0 (26.0)	15.3 (21.6)	1.7	-5.4	8.8	0.642	0.07
26 weeks	N= 176 (87-89)	22.6 (29.0)	20.2 (27.8)	2.3	-10.8	6.1	0.587	0.08
52 weeks	N= 176 (87-89)	22.5 (26.2)	20.4 (31.2)	2.1	-6.5	10.7	0.633	0.07
Painful arc present at baseline								
12 weeks	N= 128 (64-64)	12.9 (25.7)	13.1 (20.9)	-0.2	-8.4	8.1	0.971	-0.01
Painful arc absent at baseline								
12 weeks	N= 48 (23-25)	28.4 (23.6)	21.2 (22.5)	7.3	-6.1	20.7	0.280	0.32
Pain intensity reduced								
12 weeks	N= 44 (24-20)	34.5 (26.3)	34.2 (25.3)	0.4	-15.4	16.2	0.964	0.02
26 weeks	N= 110 (54-56)	26.6 (26.9)	27.3 (27.5)	-0.8	-11.0	9.5	0.885	-0.03
52 weeks	N= 114 (58-56)	30.0 (26.1)	30.7 (27.5)	-0.7	-10.7	9.2	0.886	-0.03
Pain intensity unchanged								
12 weeks	N= 132 (63-69)	10.4 (22.8)	9.9 (16.9)	0.5	-6.4	7.3	0.894	0.03
26 weeks	N= 66 (33-33)	16.1 (31.5)	8.3 (24.2)	7.8	-6.0	21.6	0.264	0.28
52 weeks	N= 62 (29-33)	7.3 (19.4)	2.8 (29.7)	4.6	-8.2	17.4	0.481	0.19

^a after unconditional mean imputation

^b 95% confidence interval of difference

^c statistically significant $P < 0.05$

withdrew from the study during the treatment period. Five and six withdrawals were registered during follow-up at 26 weeks and 52 weeks respectively (for reasons see figure 1). Data were missing for eight patients at 12 weeks and for two patients at 26 weeks.

Table 2 shows that at baseline, treatment groups were comparable on all continuous outcome

Table 4 Mean improvement on secondary outcome measures after 12, 26 and 52 weeks^a

	GET	Usual Care	Differences between groups				
	N (%)	N (%) diff	Risk lower	95% CI of diff ^b		P-value ^c	NNT ^d
				upper			
Perceived recovery (yes/no)							
12 weeks	23 (29.1)	13 (18.3)	0.11	-0.01	0.24	0.122	9
26 weeks	20 (26.7)	18 (23.7)	0.03	-0.07	0.18	0.673	33
52 weeks	25 (34.7)	18 (24.0)	0.11	-0.02	0.25	0.153	9
	GET	Usual Care	Differences between groups				
	Mean (sd)	Mean (sd) diff	Mean diff	95% CI of diff ^b		P-value	Effect-size
				lower	upper		
Shoulder pain (7-28)							
12 weeks	3.0 (3.3)	2.3 (3.4)	0.7	0.3	1.7	0.165	0.21
26 weeks	3.3 (3.7)	2.4 (4.0)	1.0	-0.2	2.1	0.096	0.25
52 weeks	7.2 (3.2)	6.6 (3.8)	0.6	-0.4	1.7	0.230	0.18
Pain intensity (0-10)							
12 weeks	1.7 (2.2)	1.5 (2.2)	0.3	-0.3	0.9	0.375	0.13
26 weeks	2.2 (2.7)	1.9 (2.2)	0.2	-0.5	1.0	0.375	0.10
52 weeks	2.5 (2.2)	1.9 (2.5)	0.6	-0.2	1.3	0.125	0.23
Quality of life (-1 to 1)							
12 weeks	0.06 (0.22)	0.06 (0.18)	0.00	0.06	-0.06	0.929	0.00
26 weeks	0.10 (0.23)	0.08 (0.16)	0.03	0.09	-0.04	0.409	0.15
52 weeks	0.10 (0.22)	0.07 (0.18)	0.03	0.09	-0.03	0.345	0.15
Fear avoidance (1-7)							
12 weeks	0.4 (1.4)	0.2 (1.0)	0.1	-0.2	0.5	0.449	0.12
26 weeks	0.7 (1.5)	0.3 (1.5)	0.4	-0.0	0.8	0.082	0.26
52 weeks	0.7 (1.4)	0.3 (1.0)	0.4	0.0	0.8	0.043	0.33
Kinesiophobia (1-7)							
12 weeks	0.2 (1.6)	0.0 (1.8)	0.2	-0.3	0.7	0.411	0.13
26 weeks	0.4 (1.6)	0.1 (1.8)	0.4	-0.2	0.9	0.201	0.21
52 weeks	0.6 (1.6)	-0.2 (1.8)	0.8	0.3	1.3	0.003	0.45
Catastrophising (1-6)							
12 weeks	0.4 (0.7)	0.2 (0.5)	0.2	0.0	0.4	0.028	0.33
26 weeks	0.4 (0.7)	0.2 (0.8)	0.1	-0.1	0.4	0.190	0.20
52 weeks	0.4 (0.7)	0.2 (0.7)	0.2	-0.0	0.4	0.053	0.29
Coping (1-6)							
12 weeks	0.1 (0.8)	-0.0 (0.7)	0.1	-0.2	0.3	0.499	0.11
26 weeks	0.0 (0.9)	0.1 (1.0)	-0.0	-0.2	0.3	0.777	0.04
52 weeks	0.1 (0.9)	0.0 (0.8)	0.1	-0.1	0.4	0.366	0.13
Internal locus of control (1-6)							
26 weeks	0.2 (0.6)	-0.0 (0.6)	0.2	-0.0	0.4	0.097	0.25
52 weeks	0.4 (1.0)	0.2 (0.9)	0.3	-0.0	0.9	0.058	0.29
External locus of control (1-6)							
26 weeks	0.3 (0.7)	0.2 (0.9)	0.0	-0.2	0.3	0.797	0.04
52 weeks	0.2 (0.9)	0.1 (0.9)	0.1	-0.2	0.4	0.405	0.13

^a after unconditional mean imputation^b 95% confidence interval of difference^c statistically significant $P < 0.05$ ^d Number Needed to Treat

measures. Patterns of treatment preferences were similar for both groups, although patients allocated to UC more frequently favoured behavioural therapy and less frequently favoured manual therapy and drugs therapy (analgesics and NSAID). Patients allocated to usual care had lower scores on the distress subscale of the 4 DSQ. These patients were less likely to report concomitant neck problems, and were more likely to report a quick onset of their current complaints. Otherwise, prognostic status at baseline was comparable for both groups. Patients eligible for analysis and patients who withdrew from the study during the treatment or follow-up period or had missing data at 12 or 26 weeks were comparable on all outcomes measures at baseline.

Overall and subgroup analyses of primary outcome measures are presented in table 3. Overall analyses show that although GET patients improved more than UC patients on both of the primary outcome measures, the differences were only statistically significant for the main complaint directly after treatment (i.e. at 12 weeks after baseline) and during follow-up at 52 weeks. Imputation did not alter these results.

Multiple regression analyses of primary outcome measures at 12, 26 and 52 weeks showed that, when adjusted for a-priori putative modifying factors (i.e. shoulder function,

Table 5. Mean utilisation of Health Care Services¹ and relevant non-health care services per patient during a one-year follow up

Type of utilisation	GET N=87 Mean (sd)	Usual Care N=89 Mean (sd)	P-value ² non-parametric ³
Direct health care services			
General practitioner (no. of visits)	0.4 (0.86)	0.8 (1.15)	0.005
Physiotherapist (no. of visits)	0.8 (2.99)	3.9 (7.04)	0.000
Manual therapist (no. of visits)	0.1 (0.48)	0.4 (1.44)	0.012
Cesar/Mensendieck exercise therapist (no. of visits)	0.0 (0.21)	0.2 (1.27)	0.040
Physician (no. of visits)	0.2 (1.00)	0.4 (1.08)	0.034
Alternative therapist (no. of visits)	0.4 (1.26)	1.0 (3.62)	0.016
Prescribed drugs (no. of prescriptions)	0.5 (1.19)	0.8 (1.82)	0.023
Relevant non-health care services			
Professional home care (no. of hours)	0.0 (0.00)	0.7 (3.81)	0.000
Paid housekeeping (no. of hours)	3.4 (17.84)	7.2 (27.72)	0.086
Unpaid help from family/friends (no. of hours)	9.7 (79.43)	1.2 (5.39)	0.144
Unpaid help from family/friends adjusted (no. of hours) ⁴	0.8 (5.63)	1.2 (5.39)	0.046
Expenses for health activities (no. of expenses)	13.0 (30.03)	17.2 (51.72)	0.553
Other out-of-pocket expenses (no. of expenses)	0.5 (1.25)	1.1 (2.27)	0.004

¹ excluding interventions (GET and UC)

² statistically significant $P < 0.05$

³ non-parametric Mann-Whitney test

⁴ adjusted for one patient reporting extremely high utilisation of unpaid help from family/friends by imputation of the group mean for utilisation of unpaid help.

anxiety, depression, somatisation and distress), baseline differences (i.e. duration of complaints, quick onset of complaints, concomitant neck problems, prior episodes of SC, treatment preferences) and recruitment strategy, the results were scarcely influenced by these variables, except for the presence of a painful arc during physical examination. Presence of a painful arc turned out to be an effect modifier. Table 3 shows that the presence of a painful arc markedly reduced the effect of GET as assessed by the SDQ after 12 weeks of treatment. GET was associated with decreases in pain intensity over time. Subgroup analyses presented in table 3 show that pain reduction was experienced by 44, 110 and 114 patients at 12, 26 and 52 weeks, respectively. GET was more effective in patients without pain reduction during the treatment.

Table 4 shows that statistically significant differences between groups as to improvement on the secondary outcome measures were only found for catastrophising (12 weeks) and for fear avoidance beliefs and kinesiophobia (52 weeks).

Table 5 shows the mean volumes of health care utilisation per patient during the one-year follow-up period. The overall utilisation of all direct health care services and relevant non-health care services during the follow-up period was lower for patients allocated to GET than for those allocated to UC (except for unpaid help from family/friends) and the difference reached statistical significance (except for paid housekeeping and expenses for health activities).

DISCUSSION

Effectiveness of GET seems to last for at least 52 weeks. The clinical differences between the GET and UC groups were rather modest, and the calculated effect sizes in this study were small (up to 0.45).

At present, there is no consensus on the outcome that is the most appropriate for shoulder complaints (Green et al 2000). Furthermore, one might argue whether or not patient centred outcomes are appropriate to evaluate effectiveness of treatments at the group level in clinical evaluation studies (Jolles et al 2005). In the 'main complaints' instrument, patients were asked at baseline to select three daily activities they regarded as most important in relation to their shoulder complaints, but not necessarily related specifically to pain. Since activities, and their relevance or importance in daily life, can vary widely between patients with shoulder complaints, and the GET programme is tailored to the patient's goals and needs, this measure is considered to be appropriate to assess the performance of daily activities in this trial. The SDQ is an instrument to assess activities in terms of functional limitations related to pain. Given the aim of the GET programme, which is not primarily to reduce pain intensity, SDQ changes might be expected to be less obvious.

Several sources of bias may have influenced the results of this study. First, since patients and health care providers could not be blinded in this study, treatment preferences of patients could have introduced bias. However, multiple regression analyses showed that treatment preferences did not influence the outcomes. Lack of blinding could also have introduced bias through differential drop-out and loss-to-follow-up rates. However, patients eligible for analyses and withdrawals were comparable at baseline and the numbers of patients that withdrew from both intervention groups were very similar. Treatment groups were comparable

with respect to outcome measures at baseline. Putative modifying factors and post-randomisation differences between groups showed no influence on primary outcome measures except for the presence of a painful arc.

One possible explanation for the modest beneficial effects found in our study may be an inadequate match between the GET programme and patient characteristics. The study population in this trial was rather heterogeneous, since only patients suffering from systemic diseases or severe medical or psychological pathology were excluded. Vlaeyen and Morley presumed that modest effect sizes in trials of behavioural treatments could be explained by a lack of knowledge about the specific biobehavioural mechanisms for the transition from acute pain to chronic pain and pain disability (Vlaeyen and Morley 2005). They suggest that the effectiveness of these treatments could be improved by a better matching between treatment and patient characteristics. Another explanation for the modest effect sizes could be the way the GET programme was administered in this trial. An earlier evaluation of the GET intervention process in this trial, using treatment registration forms filled in by the physiotherapists during treatment, evaluation forms filled in independently by physiotherapists and patients 26 weeks after the start of the treatment period, and information gathered during the focus group interview at the end of the study, showed that the process of goal-setting left some room for improvement (Geraets et al 2006). Furthermore, it showed that implementation of the programme could be facilitated when embedding the programme in a multidisciplinary primary care approach. However, the overall clinical effectiveness of GET was not influenced by flaws in the application of the programme or by lack of patient adherence. Finally, the modest effect sizes in our study could be explained by a lack of contrast between treatment groups. Firstly, one might argue whether or not the brief training courses for GPs and PTs were effective, although the supervisors (experts in the field of behavioural treatment) confirmed physiotherapists' eligibility to administer the program prior to the start of the study. Secondly, since the principles of the biopsychosocial model are nowadays more commonly applied in usual care physiotherapy, one might argue that the differences between treatments have become less distinct than intended, although none of the patients allocated to usual care was treated with behavioural therapy as such.

To our knowledge, this is the first trial on the effectiveness of a behavioural exercise programme for chronic shoulder complaints in a primary care setting administered by a PT. Earlier studies mainly focused on the effectiveness of these treatments for other chronic pain patients, viz. those with chronic low back pain. Moreover, the behavioural exercise programmes evaluated in earlier studies were mostly embedded in multidisciplinary cognitive-behavioural programmes and in secondary settings (Morley et al 1999, Tulder et al 2001). The content and the effectiveness of the GET programme cannot be compared with more comprehensive multidisciplinary programmes or operant treatment packages administered by the psychologist.

The GET programme is based on the principles of graded activity, operant conditioning and time contingency, and aims at restoring patients' own preferred daily activities, rather than primarily at pain reduction. Therefore, we firstly assumed that pain behaviour and pain-related inactivity would be modified in accordance with learning theory principles during the treatment period, i.e., through new learning experiences, reinforcement, rewarding, goal setting and levels of activity gradually increasing over time (Skinner 1953, Fordyce 1976). This assumption was confirmed by our short-term results on primary outcome measures after 12 weeks of treatment, although the differences between the groups were only

statistically significant for main complaints. Secondly, we assumed these behavioural changes to be consolidated after the treatment period. We assume that once behaviour has changed in the preferred direction and patients experience the progress made as a consequence of their own healthy behaviour, they will become more motivated to succeed in performing and maintaining the preferred activities. Furthermore, we expected that the special attention paid to the application of what has been learned in everyday life, would lead to improvements in the performance of daily activities after the treatment period. Our present findings confirm that differences between the treatment groups on the primary outcome measures remain significant after 52 weeks of follow-up. Furthermore, utilisation of health care services and non health care services during 52 weeks of follow-up was lower for patients allocated to GET. Patients allocated to GET had significantly higher scores for improvement on pain-catastrophising and pain-related fear in the long term. We assume that, even though GET is a behavioural treatment (and not a cognitive treatment), positive experiences in performing daily activities during treatment may not only have contributed to improvements in the performance of daily activities, but also to reduction of pain-catastrophising and pain-related fear in the long term. These findings are in line with earlier studies on chronic low back pain patients in which catastrophising thoughts and fear of movement were associated with the performance of activities (Vlaeyen 1999).

Patients allocated to GET showed greater improvement in the performance of daily activities, irrespective of perceived recovery after 12, 26 and 52 weeks. These results imply that patients allocated to GET were less likely to consider their ability to perform daily activities at home or at work to be dependent on perceived recovery or pain experience, which is in line with the concepts of the GET programme.

A question that remains is which patients might benefit most from GET. The present trial included a broad range of patients with shoulder complaints. Analysis showed that the presence of a painful arc during physical examination at baseline minimised the effectiveness of GET. Painful arc is a well-known sign associated with sub-acromial impingement, as the initial stage of rotator cuff injuries (characterised by inflammation of the tendon), with rotator cuff tears as the final stage (Neer and Welsh 1977). Numerous causes, contributing factors and possible therapeutic options for shoulder impingement have been reported (Pyne 2004). Furthermore, GET seemed to be more effective in patients not reporting pain reduction during the treatment period. We expected that pain reduction over time would lead to improvements in the performance of daily activities as a natural course. Since the aim of GET is not primarily to reduce pain intensity, we assumed that GET would be more effective in patients not reporting pain reduction over time. Explorative subgroup analyses on pain reduction in patients confirmed this assumption. A recent study on shoulder complaints in primary care showed that high pain intensity scores at baseline predict a poorer long-term outcome (Kuipers et al 2004). More generally, chronic pain research has shown that pain-catastrophising, pain anxiety and pain-related fear seem to be associated with over-predicting actual pain and under-predicting abilities to perform physical tasks and to adjust pain behaviour (Keefe et al 2004).

Based on our study we recommend that GET should not be used for patients with a painful arc. More research on the phenomenon of a painful arc is needed to elucidate the value of exercise programmes in general for patients with shoulder impingement. Predicting which patients are at risk for persistent shoulder pain in the long term is of great interest to achieve a better match between the GET programme and patient characteristics. We suggest

that more research is needed on the cognitive and behavioural aspects of pain-predicting in patients with chronic shoulder pain, as it could provide new insights into the prognosis and course of complaints.

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CHAPTER 5

Cost-effectiveness

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Cost-effectiveness of a graded exercise therapy programme for patients with chronic shoulder complaints. Geraets JJXR, Goossens MEJB, de Bruijn CPC, de Groot IJM, Köke AJA, Pelt RAGB, van der Heijden GJMG, Dinant GJ, van den Heuvel WJA. *Int J Technology Assess Health Care* 2006.

ABSTRACT

Objectives: The present study evaluated the cost-effectiveness of a behavioural Graded Exercise Therapy (GET) programme compared to usual care (UC) in terms of the performance of daily activities by patients with chronic shoulder complaints in primary care.

Methods: One-hundred-and-seventy-six patients were randomly assigned either to GET (N=87) or to UC (N=89). Clinical outcomes (main complaints, shoulder disability (SDQ) and generic health-related quality of life (EQ5D)) and costs (intervention costs, direct health care costs, direct non-health related costs and indirect costs) were assessed during the 12-week treatment period and 52 weeks of follow-up.

Results: Results showed that GET was more effective than UC in restoring daily activities as assessed by the main complaints instrument after the 12-week treatment period ($p=0.049$; mean difference 7.5; CI 0.0-15.0). These effects lasted for at least 52 weeks ($p=0.025$; mean difference 9.2; CI 1.2-17.3). No statistically significant differences were found on the SDQ or EQ5D. GET significantly reduced direct health care costs ($p=0.000$) and direct non-health care costs ($p=0.029$). Nevertheless, total costs during the one-year follow-up period were significantly higher ($p=0.001$; GET € 530 versus UC € 377) due to the higher costs of the intervention. Incremental cost-effectiveness ratios for the main complaints (0-100), SDQ (0-100) and EQ5D (-1.0 – 1.0) were € 17, € 74, and € 5278 per unit of improvement respectively.

Conclusion: GET proved to be more effective in the short and long term and reduces direct health care costs and direct non-health care costs, but is associated with higher costs of the intervention itself.

Key words: cost-benefit analysis, shoulder, behavior therapy, randomized controlled trials.

INTRODUCTION

Shoulder complaints (SC) are serious musculoskeletal problems because of their occurrence, course, and persistence (Luime 2004). Patients with shoulder complaints suffer from pain and limitations in the performance of daily activities (Picavet et al 2003). Besides personal suffering, chronic shoulder complaints entail a huge social and economic burden due to patients' inability to carry out household tasks, loss of productivity, sick leave and/or utilisation of health care services. Musculoskeletal disorders, of which SC constitute the second largest group after low back disorders, account for the second largest share in healthcare costs in the Netherlands (Meerding et al 1998). In Sweden, 18% of disability payments made for musculoskeletal disorders relate to shoulder complaints (Nygren et al 1995).

In the past decade, increasing attention has been focused on economic evaluations regarding patients with musculoskeletal disorders, alongside clinical effectiveness studies. Remarkably, costs for low back pain patients are not normally distributed: most expenses (more than 80%) are incurred for a minority of patients (less than 25%) in whom low back pain develops into a chronic disorder (Goossens et al 1997, Waddell 1998). Hence, preventing chronic musculoskeletal disorders and improving abilities and healthy behaviours in pain patients at an earlier stage should be able to reduce costs to health care and society.

Behavioural treatments have proved to be effective in the treatment of chronic pain patients in multidisciplinary secondary and tertiary settings (Morley et al 1999, Guzman et al 2001, Tulder et al 2001).

We have developed a behavioural Graded Exercise Therapy (GET) programme to improve the performance of daily activities irrespective of pain experiences in patients with chronic shoulder complaints in primary care settings. The clinical effectiveness of this programme was proved in an earlier study (Geraets et al 2005). We assumed that improved abilities and behavioural changes would also contribute to a reduction in costs of health care services and in costs due to loss of productivity or sick leave. This study was done for three reasons: first, to evaluate the clinical effectiveness of the GET programme compared to usual care; second, to evaluate the costs (intervention costs, direct health care costs, direct non-health related costs, and indirect costs) for both treatment groups; third, to evaluate the cost-effectiveness from a societal perspective for both treatment groups. To our knowledge, this is the first study on the cost-effectiveness of behavioural treatment in patients with chronic shoulder complaints in primary care.

METHODS

Study population

Patients with chronic SC living in the Province of Limburg (the Netherlands) were invited to participate in the study either during consultation with their general practitioner (GP) for chronic shoulder complaints or by advertisement in a local newspaper between January 2002 and July 2003. Patients were included if they were at least 18 years old and had been suffering from SC for at least three months. Patients suffering from systemic diseases, referred pain or severe biomedical or psychiatric disorders were excluded. The study design was approved by the iRv/SRL's Medical Research Ethics Committee.

Interventions

Eligible patients were randomised and allocated either to Graded Exercise Therapy (GET) or to usual care (UC). GET is a behavioural treatment programme characterised by graded activity, time-contingency and operant conditioning, which was administered by 20 physiotherapists (PTs). The programme consists of a maximum of 18 group sessions of approximately 60 minutes over a period of 12 weeks. The content of the GET programme has been described in detail elsewhere (Geraets et al 2004). Usual care was standardised according to the 1999 version of the guidelines for SC issued by the Dutch College of General Practitioners (DCGP) (Winters et al 1999b; see also <http://nhg.artsennet.nl/upload/104/guidelines2/E08.htm>). UC consists of information, recommendations and pain-contingent medical or drug therapy. UC was administered by 32 practitioners. In UC, it was the general practitioners who decided on the specific treatment.

Clinical outcome measures

Primary outcome measures to assess the performance of daily activities were the 'main complaints' instrument and the Shoulder Disability Questionnaire (SDQ) (Beurskens et al 1999, Heijden van der et al 2000). In the 'main complaints' instrument, patients selected, at baseline, the three most important daily activities that were affected by their SC. They rated their ability to perform these activities during the past week on an ordinal (eleven-point) scale at baseline and during follow-up. The SDQ is a functional status measure consisting of 16 statements regarding pain and limitations to daily activities during the past 24 hours. Generic health-related quality of life was assessed and rated on the EuroQol-5D (EQ5D) (Brooks 1996). The EQ5D consists of a descriptive system for health status, related to five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/ depression) and a visual analogue scale. Measurements took place at baseline, directly after the 12-week treatment period and after 52 weeks of follow-up.

Costs

Intervention costs, direct health care costs, direct non-health related costs, and indirect costs were assessed during the 12-week treatment period and the 52-week follow-up period. The intervention costs of the GET programme included the costs of visits to physiotherapists for group treatment during the 12-week treatment period. The intervention costs for UC included the costs of visits to general practitioners, to physiotherapists for usual care or to manual therapists or Cesar/Mensendieck exercise therapists during the 12-week intervention period. Other direct health related costs for both treatment groups during the 12-week treatment period included the costs of prescribed medication, of hospitalisation and of visits to physicians or alternative therapists. Direct health related costs after the treatment period included the costs of visits to general practitioners, physiotherapists, manual therapists, Cesar/Mensendieck exercise therapists, physicians and/or alternative therapists, costs of hospitalisation and costs of prescribed medication during the 52-week follow-up period. Direct non-health related costs included costs of professional home care, of paid housekeeping, of unpaid help from relatives or friends, of health-related activities (e.g. fitness training) and other out-of-pocket expenses (e.g. non-prescribed medication). Indirect costs included the costs of production losses due to sick leave from paid or unpaid work.

Physiotherapists documented the number of visits by patients allocated to GET on a registration form (Geraets et al 2006). Cost diaries filled in by the patients were used to assess direct health care costs, direct non-health related costs and indirect costs (Goossens et al 2000). The cost diaries were sent to the patients by post. Two strategies were used to collect the cost data. Patients were allocated at random to a group recording their weekly expenses continuously in ten diary booklets covering the 52-week period or to a group recording them intermittently in seven diary booklets, covering two weeks out of each eight-week period (fourteen weeks in total during the 52-week follow-up period). We did this to answer an addition methodological question, viz., whether keeping a diary for an intermittent period would yield different results than keeping one for the total follow-up period of one year. We found no significant difference between the two assessment strategies ($p=0.890$), which means that both could be used to calculate the final cost data. Patients returned the diaries immediately after each booklet had been completed.

Prices of visits to health care providers, hospitalisation, professional home care and paid housekeeping were obtained from the guidelines for economic evaluation in health care by the Dutch Health Care Insurance Counsel (Oostenbrink et al 2004). Prices of visits to alternative therapists were obtained from professional organisations or from the cost diary. Prices of prescribed or non-prescribed medication were obtained from the Royal Dutch Society for Pharmacy or from the cost diaries. Prices of unpaid help from family/friends and sick leave from unpaid work were based on shadow prices for unpaid work (Oostenbrink et al 2004). The Human Capital Approach was used to calculate the costs of sick leave from paid work (Oostenbrink et al 2004).

Statistical analysis

Analyses were performed according to the intention-to-treat principle, using SPSS statistical software (12.0.1 version). A p -value of <0.05 was considered to be statistically significant (two-tailed) for all comparisons.

Change scores on clinical outcome measures were calculated (follow-up scores minus baseline scores), as well as mean differences between treatment groups and 95% confidence intervals. Paired-sample Student's t -tests were used to test for significant differences between groups on continuous scales having a Gaussian distribution. If data were missing, unconditional imputation of the overall mean was applied.

Differences between groups in utilisation of health care services were calculated for both intervention groups. Mean costs per treatment group and mean differences between groups were analysed. As cost data are usually highly skewed, non-parametric Mann-Whitney tests for non-Gaussian distributions were used to test for significant differences between groups. If data were missing, individual mean imputation was applied. If no cost data were available, we used unconditional imputation of the group mean.

Incremental cost-effectiveness ratios (the ratio between the difference in costs and the difference in clinical effects) were calculated by bias-corrected bootstrapping (using 1000 replications) (O'Brien and Briggs 2002, Campbell and Torgerson 1999). Cost-effectiveness ratios for both of the primary outcome measures (main complaints and SDQ) and for health-related quality of life (EQ5D) were plotted on a cost-effectiveness plane.

Alternative cost analyses were performed to evaluate the influence of outliers for the utilisation of health care services on outcomes.

RESULTS

Study population

A total of 176 patients were randomised and allocated to either Graded Exercise Therapy (GET) (N=87) or usual care (UC) (N=89). Eighteen patients (10%) withdrew from the study during the treatment period, while 11 (6%) withdrawals were registered during the 52-week follow-up period. Eighty-nine patients (GET= 41; UC= 48) filled in the diaries continuously, while 87 patients (GET = 46; UC = 41) filled in the diaries intermittently. One hundred and two patients (58%) completed and returned all cost diaries. No cost data were available for the 15 withdrawals (9%). Overall, 1213 out of a total of 1499 (81%) cost diaries were returned during the 52-week follow-up period.

Baseline

Treatment groups were comparable at baseline in terms of patient characteristics and clinical outcome measures (table 1). The numbers of patients who reported having paid work were similar for both treatment groups (GET 57%; UC 59%). Sick leave from paid work at baseline (if applicable) extending a one-week period during the past eight weeks was reported by 4% of the patients allocated to GET and by 12% of the patients allocated to

Table 1. Valuation of health care volumes (in €)

Direct Health Care Costs	
General practitioner (per visit)	20.20 ¹
Physiotherapist (per visit)	22.75 ¹
Manual therapist (per visit)	32.20 ¹
Cesar/Mensendieck exercise therapist (per contact)	23.00 ¹
Physician (per visit)	56.00 ¹
Alternative therapist (per visit)	Variable ²
Hospitalisation (per day)	337.00 ¹
Prescribed drugs (e.g. analgetics and nsaid)	Variable ³
Direct Non-Health Care Costs	
Professional home care (per hour)	26.70 ¹
Paid housekeeping (per hour)	12.70 ¹
Unpaid help from family/friends (per hour)	8.30 ⁴
Expenses for health activities (e.g. fitness)	Variable ²
Other out-of-pocket expenses (e.g. non-prescribed drugs)	Variable ³
Indirect Costs	
Sick leave from paid work (per day)	HCA ⁵
Sick leave from unpaid work (per hour)	8.30 ⁴

¹ prices obtained from the Health Care Insurance Board (Oostenbrink et al 2004)

² prices as indicated by patients in the cost diaries

³ prices obtained from the Royal Dutch Society for Pharmacy

⁴ based on shadow prices for unpaid work (Oostenbrink et al 2004)

⁵ Human Capital Approach (Oostenbrink et al 2004)

UC. Furthermore, patients eligible for analysis and patients who withdrew from the study or had missing data during the treatment or follow-up periods were comparable on all outcomes measures at baseline.

Clinical effectiveness

Table 1 shows that GET patients had improved more than UC patients on both primary outcome measures (main complaint and SDQ) immediately after the 12-week treatment and after 52 weeks of follow-up, although the differences were only statistically significant for the main complaint. No statistically significant differences between groups were found as regards improvement in quality of life (EQ5D). Imputation did not alter these results.

Health care utilisation and sick leave

Table 2 shows the mean volumes of health care utilisation per patient during the one-year follow-up period (excluding GET and UC). The overall utilisation of all direct health care services and relevant non-health care services during the follow-up period was lower for patients allocated to GET than for those allocated to UC (except for unpaid help from family/friends) and the difference reached statistical significance (except for paid housekeeping and expenses for health activities). There was also a statistically significant difference in sick leave from unpaid work during follow-up in favour of GET. No statistically significant differences between the treatment groups were found in sick leave from paid work.

Table 2. Baseline characteristics

	GET N=87	Usual Care N=89
Demographic variables		
Mean age (years) (sd)	51(13.1)	53 (11.7)
Female (%)	51	58
Paid work (%)	56	57
Sick leave (if paid work) in past 8 weeks (> 1 week) (%)	4	12
Outcome variables Mean (sd)		
Severity of main complaints (0-100)	76.2 (19.18)	71.9 (19.6)
Functional limitations in daily activities (SDQ) (0-100)	66.0 (18.06)	65.6 (19.86)
Quality of life (EQ5D) (-1 to 1)	0.66 (0.234)	0.69 (0.198)

Costs

The mean costs per treatment group are presented in table 3. The intervention costs for the GET programme were based on an average of 17.2 sessions per patient. The intervention costs for GET (€ 261) were significantly higher than those for UC (€ 61). Patients allocated to GET had significantly higher total costs during the 12-week treatment period and significantly lower costs during the follow-up period (weeks 12-52) than patients allocated to UC. Total mean costs over the entire 52-week period of treatment plus follow-up were € 153 higher for patients allocated to GET.

Table 3. Mean improvement per outcome measure after 12 and 52 weeks¹

	GET N=87	Usual Care N=89	Differences between groups			
	Mean (sd)	Mean (sd)	Mean diff	95% CI of diff ²		P-value Parametric ³
				lower	upper	
Main complaints (0-100)						
12 weeks	32.8 (25.7)	25.3 (24.5)	7.5	0.0	15.0	0.049⁴
52 weeks	41.1 (26.7)	31.8 (27.4)	9.2	1.2	17.3	0.025⁴
SDQ (0-100)						
12 weeks	17.0 (26.0)	15.3 (21.6)	1.7	-5.4	8.8	0.642
52 weeks	22.5 (26.2)	20.4 (31.2)	2.1	-6.5	10.7	0.633
Quality of life (-1 to 1)						
12 weeks	0.06 (0.22)	0.06 (0.18)	0.00	-0.06	0.06	0.929
52 weeks	0.10 (0.22)	0.07 (0.18)	0.03	-0.03	0.09	0.345

¹ after unconditional mean imputation

² 95% confidence interval of difference

³ parametric Student's t-test

⁴ statistically significant P<0.05

Cost-effectiveness analysis

The incremental cost-effectiveness ratios (CER) for the severity of the main complaints (0 - 100), SDQ (0-100) and EQ5D (-1.00 – 1.00) after 52 weeks indicate that the incremental costs for GET per unit improvement on these outcome measures were € 17 (CI - 4 -129), € 74 (CI -2-101) and € 5278 (CI -11.808-51.407), respectively.

Figure 1. Cost-effectiveness plane for the main complaints after 52 weeks

The cost-effectiveness plane for the main complaints instrument after 52 weeks of follow-up is shown in figure 1. This plane shows that most cost-effect pairs (91%) are in the upper-right quadrant, indicating positive effects at higher costs. Cost-effectiveness planes for the SDQ and EQ5D showed similar patterns, although more cost-effect pairs were located near the vertical axis, indicating smaller clinical effects at higher costs (no data presented).

Sensitivity analysis

Alternative analyses were performed after imputation of the group mean for one patient who reported extremely high utilisation of unpaid help from relatives/friends. After adjustment for this outlier, utilisation of all direct non-health care services was lower for patients allocated to GET than for those allocated to UC (table 2). Adjusted total mean costs were 79 higher for patients allocated to GET (table 3). The adjusted incremental cost-effectiveness ratios for the severity of the main complaints, SDQ and EQ5D after 52 weeks were € 9 (CI 6-16), € 40 (CI -4-57) and € 2846 (CI -2.765-3.763), respectively.

DISCUSSION

GET patients showed statistically significantly greater improvement than UC patients on the main complaint instrument directly after the 12-week treatment, and these improvements lasted for at least 52 weeks. Improvements on the SDQ were greater with GET than with UC, but the differences between the groups never reached statistical significance. No statistically significant differences were found on the EQ5D. Patients allocated to GET showed statistically significantly lower direct health care costs and direct non-health care costs during the follow-up period (week 12-52) compared to patients allocated to UC. Nevertheless, since the costs of the GET programme were higher than those of UC, total costs for GET patients were significantly higher than for UC patients.

As expected, GET significantly improved the performance of daily activities as assessed by the main complaints measure. This means that patients' ability to perform the three most important daily activities improved significantly, both in the short term and after one year of follow-up. However, the SDQ, which measures pain and functional limitations in daily activities, did not show a significant difference between the GET and UC groups. Since the aim of GET is to improve the performance of daily activities irrespective of pain experiences, changes measured on the SDQ might be expected to be relatively small. No statistically significant differences were found on the five dimensions of the EQ5D measured at a three-point level. It is very likely that improvements in individual daily activities due to GET were too specific to be detected by this generic health-related quality of life measure.

Patients were taught self-management of their complaints and how to deal with a new episode of shoulder complaints. We hypothesised that behavioural changes during the treatment period, relating to improvement of self management due to GET, would reduce the utilisation of health care services during the follow-up period and reduce sick leave in patients allocated to GET. The results show that the utilisation of health care services during the follow-up period was indeed significantly lower in patients allocated to GET. However, there was no statistically significant difference between groups regarding sick leave from paid work. The first reason for this was the low number of patients that reported sick leave from paid work in both groups (11 in GET versus 15 in UC), so these results need to be interpreted with considerable caution. A related explanation could be that return to work was not an

explicit aim in this study. Patients were asked to identify daily activities that interrupted their daily lives and the ones they preferred to improve. These goals were not predominantly related to work and patients were only stimulated to apply to their work settings what they had learned from the therapy.

As expected, the intervention costs of the GET programme (€ 268) were significantly higher than those of UC (€ 61). This difference is mainly accounted for by the number of visits to physiotherapists for group treatment (on average 17.2 visits) compared to the number of visits to other health care providers (general practitioners, physiotherapists, manual therapists and Cesar/Mensendieck exercise therapists), mainly accounts for these differences. The incremental cost-effectiveness ratio (CER) of the main complaints instrument, for GET compared to UC, shows that it costs € 17 to increase performance of daily activities with 1 %. Recently the CER of the main complaints instrument, for manipulative therapy as add-on to UC compared to UC alone was calculated at € 22 for a 1% increase in the performance of daily activities in patients with shoulder complaints and concomitant neck problems (Bergman et al 2005). This indicates that cost-effectiveness ratios for GET in patients with chronic shoulder complaints and for manipulative therapy as an add-on to UC in patients with shoulder complaints and concomitant neck problems are comparable. The costs per patient to improve the performance of daily activities by 25%, which was the aim of this trial, were calculated to be € 425. When adjusted for one outlier these costs were € 225.

We conclude that GET is more cost-effective than UC for patients with chronic shoulder complaints in primary care. GET is clinically more effective than UC in restoring daily activities in these patients after the 12-week treatment period, and these effects last for at least 52 weeks. GET significantly reduces direct health care costs and direct non-health care costs in patients with chronic shoulder complaints. However, total costs during the one-year follow-up period were significantly higher due to the higher costs of the intervention itself.

POLICY IMPLICATIONS

It is recommended to use GET to restore daily activities in patients with chronic shoulder complaints in primary care. GET is effective in restoring daily activities in patients with chronic shoulder complaints in long term in a primary care setting and might as such prevent more intensive and more expensive multidisciplinary treatment of these patients in secondary or tertiary care settings. We recommend that the programme should focus more on work-related goals and work-related activities in patients having paid work, which might improve the social benefits of GET.

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Chapter 5

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CHAPTER 6

Process evaluation

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ABSTRACT

Objective: The intervention process was evaluated in a randomised clinical trial on the effectiveness of a behavioural Graded Exercise Therapy (GET) programme for patients with chronic shoulder complaints in primary care settings. This process evaluation was done for three reasons: first, to know whether the programme was performed as planned, second, to know whether or not this treatment is feasible in normal practice, and third, to identify needs for improvement of the protocol to facilitate implication.

Methods: We evaluated the extent to which the programme is being applied according to protocol, patient adherence to the programme, and the suitability of the programme according to patients and physiotherapists. Twenty participating physiotherapists and 87 patients allocated to GET were asked to evaluate the intervention process. Furthermore, a sample of ten patients, taken from the total number of 87 patients allocated to GET, was invited to take part in a focus group interview at the end of the study. We evaluated the intervention process using a treatment registration form filled in by the physiotherapists during treatment, evaluation forms filled in independently by physiotherapists and patients 26 weeks after the start of the treatment period, and information gathered during the focus group interview at the end of the study.

Results: GET was applied according to protocol to an acceptable extent, and participating patients showed satisfactory adherence to the programme.

Conclusions: Clinical effectiveness of GET in this trial is not influenced by flaws in the application of the programme or by lack of patient adherence.

Practice implications: The programme could be improved in terms of the process of goal-setting, and the implementation of GET could be facilitated if the programme is embedded in a multidisciplinary approach in primary care.

Key words: Evaluation study, shoulder complaints, behavioural therapy, randomised clinical trial.

INTRODUCTION

In the past decade, increasing attention is being paid to quality of life outcomes and cost-effectiveness of treatment programmes, in order to support policy decisions (Gerszten 1998, Urden 2002). Unfortunately, however, still little attention is paid to the evaluation of the intervention process in trials (Haastregt et al 2002). Effectiveness of a treatment under study is not only determined by its content, but also by its application and by participants' experiences, adherence, beliefs and attitudes (Kvien and Heiberg 2003, Thomas et al 2004, Goossens et al 2005, Jensen et al 2004, Keefe et al 2004, Lackner et al 1996, Keith 1998, Westbrook et al 1993). Therefore, information on the intervention process is essential for the interpretation of the results of a trial (Haastregt et al 2002). For example, if an intervention turns out to be ineffective or less effective than expected, this could be due to weaknesses in or unsuitability of the intervention, but also to flaws in its application (protocol deviations). In addition, gathering information about the intervention process is useful for further improvement of the intervention and for its implementation in regular practice when it proves successful.

This process evaluation study was embedded in a trial on clinical effectiveness of a Graded Exercise Therapy (GET) programme in patients with chronic shoulder complaints in a primary care setting. Shoulder complaints (SC) are a major health problem in the Netherlands. In 1998, the prevalence of chronic SC lasting more than three months in the Dutch general population (upwards of 25 years of age) was 15% (Picavet and Schouten 2003). Patients with chronic SC suffer from disability and pain (van der Heijden 1999). About a quarter (27%) of all patients with SC report persisting pain, and 29% mention limitations in the performance of daily activities (Picavet and Schouten 2003). Approximately 50% of all patients with SC still have complaints 6 months after their first visit to the General Practitioner (GP), despite treatment as usual (van der Windt et al 1996).

Because SC can have a considerable impact on daily life and often develops into a chronic disorder, it is important to assess options for further optimising the treatment of patients with SC. In the last decades, behavioural therapy principles have proven to be effective in the management of musculoskeletal pain problems among low back pain patients (Guzmán et al 2001, Linton 1999, Morley et al 1999, van Tulder et al 2001, Vlaeyen and Linton 2000). It is likely that behavioural therapy will also be effective in the treatment of patients with chronic SC (Linton 1995), although specific evidence on this issue is still lacking. We therefore developed a GET programme for chronic SC patients (Geraets et al 2004). This behavioural programme is administered by a physiotherapist (PT). The programme is currently being evaluated on its effectiveness and cost-effectiveness in a randomised clinical trial. GET is compared with usual care for SC according to the guideline for shoulder complaints issued by the Dutch College of General Practitioners (DCGP) in 1999 (Winters et al 1999).

The present process evaluation was done for three reasons: first, to know whether the GET programme was performed as planned, second, to know whether or not this treatment is feasible in normal practice, and third, to identify needs for improvement of the protocol to facilitate implication. Therefore, we describe the extent to which the intervention is being applied according to protocol, the adherence of patients to the programme, and the suitability of the programme according to patients and physiotherapists.

GRADED EXERCISE THERAPY

GET is a behavioural programme developed for chronic SC in a primary care setting, administered by a physiotherapist. The main elements of the programme are listed in table 1.

Table 1. Main elements of the Graded Exercise Therapy programme

Start-up period (approximately 6 sessions over a 2-week period)
<ul style="list-style-type: none"> • Rationale: Prior to the start of the programme, patients receive a short brochure explaining the rationale behind it. • Reconceptualisation: Pain and pain-related disability are reviewed to ensure that patients are convinced they are able to control and influence their pain experience and improve levels of activity. • Goal-setting: Treatment goals are set, related to the patient's own preferred daily activities.
Treatment plus generalisation period (approximately 12 sessions over a 10-week period)
<ul style="list-style-type: none"> • Graded Activity: Levels of activity are increased in a step-wise fashion. • Time contingency: Levels of activity are structured in time and not according to pain experience. • Operant conditioning: Environmental reinforcement is used to promote and improve healthy behaviour. • Generalisation: What has been learned is applied to everyday life.

An important aim of GET is to increase levels of daily activity by learning from the consequences of behaviours. Pain behaviour is expected to be consolidated when patients experience the consequences of this behaviour as pleasant and to extinguish when they experience it as unpleasant. Operant learning principles are used to promote and improve healthy behaviour by changing the consequences of behaviour (Fordyce 1976, Skinner 1953). Positive reinforcement of the preferred behavioural changes is given to increase and maintain the desired behaviour. In graded activity, levels of activity increase in a step-wise time-contingent fashion. This means that the intensity of exercises increases gradually over time, irrespective of pain experience, towards preset goals and with fixed quota agreed upon at the start of the programme. The GET programme consists of a maximum of 18 group sessions of approximately 60 minutes over a period of 12 weeks. GET is administered in small groups of three to five persons. During the 'start-up period', the rationale is explained, pain and pain-related disability are discussed, baseline levels of activities are established, and treatment goals are set. The 'treatment plus generalisation' period involves the performance of operant conditioning and time-contingent graded exercises. At the start of the programme, the frequency of sessions is fixed at three times a week, after which it gradually decreases to one session every two weeks. Generalisation to everyday life is strongly emphasized at the end of this phase.

Prior to the start of the study, physiotherapists participating in the GET group took part in a one-day workshop and two booster sessions under the supervision of experts in the field of cognitive-behavioural treatment. More details of the development and content of GET have been presented elsewhere (Geraets et al 2004).

METHODS

Participants

Patients were eligible for participation in the randomised clinical trial if they had suffered from shoulder complaints for at least three months. Patients suffering from systemic diseases,

referred pain or severe biomedical or psychiatric disorders were excluded. Since we considered PT experience as a putative prognostic factor, participants were pre-stratified at the level of the nearest physiotherapy practice before randomisation. Eighty-nine patients were allocated to the control group (usual care by the general practitioner). Because these patients did not receive the GET-programme they did not participate in the process-evaluation. Eighty-seven patients were allocated to the GET programme administered on ten locations by twenty physiotherapists (two physiotherapists per location). All patients allocated to the intervention group and all physiotherapists who administered the GET programme, were asked to participate in the process evaluation. We divided the participating patients into two subgroups that either completed the programme (maximum of 18 sessions or fewer than 18 sessions and no more shoulder complaints at the time the treatment was ended) or did not complete the programme (fewer than 18 sessions and still having shoulder complaints when the treatment was ended).

Outcome measures

Application of the programme according to protocol

In order to determine whether the GET programme was being applied according to protocol, we assessed the number of treatment sessions and the duration of the programme by means of a registration form (A) filled in by the physiotherapists during the intervention period (table 2, items 1.1 and 1.2). In addition, application of the main elements of the programme was assessed by means of registration form (A) and concealed evaluation forms (B and C), filled in independently by all participating physiotherapists (A and B) and patients (C) 26 weeks after the start of the programme. Physiotherapists and patients received the evaluation forms (B and C) by post and were asked independently whether the main elements of the programme as listed in table 2 (item 1.3) had been reviewed or applied during the programme. All items were formulated as statements which had to be rated on a five-point ordinal scale (ranging from 1 = fully convinced to 5 = not at all convinced).

Programme adherence by participants

In order to assess adherence by participants, the physiotherapists were asked to rate on a five-point ordinal scale whether they were satisfied with the way their patients had participated in the programme, and the patients were asked whether they were satisfied with the way they had participated in the programme (table 2, item 2).

Suitability of the programme

In order to assess the suitability of the programme, physiotherapists were asked to rate on a five-point ordinal scale whether they considered GET to be suitable for the complaints of each participating patient. In addition, each patient was asked to rate whether he or she had experienced GET to be a suitable treatment for their own SC (table 2, item 3).

Focus group interview

A sample of ten patients, taken from all patients allocated to GET, was asked to take part in a focus group interview at the end of the intervention period. We aimed at selecting a representative group of all GET patients to participate in this interview. Patients were selected on age and sex, as well as on the physiotherapy practice to which patients had been allocated, in order to gather information from individual strata of the trial. Furthermore, the focus

group included both patients who had completed the GET programme and patients who had not completed the programme. Matched substitutes were selected if patients were not willing to participate. The aim of this semi-structured interview was to gain additional qualitative information on the most important aspects of the intervention process (table 2). An independent interviewer who was not involved in conducting the trial supervised the intervention. Data were recorded on a form (D) by a research assistant.

Analysis

Means and standard deviations were calculated for continuous baseline and outcome variables. Medians and cumulative percentage scores were used for ordinal variables (items of the evaluation forms). Qualitative data on the intervention process were analysed and main outcomes are presented.

RESULTS

Participants

All twenty physiotherapists filled in registration forms A and evaluation forms B.

Eighty-seven patients were allocated to GET in this trial. Six patients withdrew from the study within 26 weeks of follow-up (one patient because of the frequency of the sessions, one because of a different treatment preference, one because of neck problems, one for private reasons, one for lack of time and one because of unwillingness to participate in the study any longer). Eighty-one patients were asked to fill in evaluation form C. Seventy-eight patients (96%) returned this form and participated in the process evaluation.

Characteristics of participants are listed in table 3. Demographic variables, specific disease variables, outcome or process variables, and treatment preferences for patients who participated in the process evaluation were comparable to patients who did not participate. The small group (N=9) who did not participate in the process evaluations included slightly younger patients, had less concomitant neck problems, and the duration of their complaints was shorter. Five patients who participated in this process evaluation had not completed the GET programme (one for other medical reasons, one for psychological reasons, one because of a trauma, and two because of increased complaints). Table 3 shows that characteristics of patients who completed the programme and those who did not complete the programme were comparable, although the small group who did not complete the programme (N=5) included more female patients, had less concomitant neck problems, and were more ambivalent in their opinion about physiotherapy.

The items relating to the application of the main elements of the intervention were only rated by the 73 patients who completed the programme. In addition, adherence to the programme and suitability of the programme could not be assessed for one of the patients, who did not complete the programme and ended treatment after one session.

Nine of the ten patients who had been invited to the focus group interview at the end of the intervention period actually participated in the interview (one patient cancelled her appointment at the last minute for medical reasons). These patients had been allocated to seven different physiotherapy practices. Seven of these patients had fully completed the programme. Table 3 shows that characteristics of patients who participated in the focus group were comparable to those of all patients allocated to GET.

Table 2. Outcome measure

	Physiotherapists		Patients	
	Registration forms ^a A	Evaluation forms ^b B	Evaluation forms ^b C	Focus group interview ^c D
1. Application according to protocol				
1.1 Number of sessions	X			
1.2 Duration of programme	X			
1.3 Main elements of treatment				
Rationale				
- Rationale of GET explained				X
Reconceptualisation				
- Pain-related disability reviewed		X	X	X
- Pain beliefs reviewed		X	X	X
- Environmental factors at home and at work reviewed		X	X	X
- Main complaint reviewed		X	X	X
- Barriers and obstacles towards recovery reviewed		X	X	X
Goal-setting				
- Treatment goals defined	X	X	X	X
Graded activity				
- Levels of activities increased stepwise	X	X	X	X
Time contingency				
- Levels of activities structured in time	X	X	X	X
Operant conditioning				
- Reinforcement of pain control behaviours		X	X	X
- Reinforcement of pain-related activities		X	X	X
Generalisation				
- Self-management of complaints reviewed		X	X	X
- Setting of new goals reviewed		X	X	X
- Application of treatment principles after treatment period reviewed		X	X	X
2. Adherence to the programme				
- PT's satisfaction with the way the patient participated in the programme		X		
- Patient's satisfaction with the way he or she participated in the programme			X	X
3. Suitability of the programme				
- Suitability of the programme for SC of patient as perceived by PT		X		
- Suitability of the programme for own SC as perceived by patient			X	X

^a Filled in during treatment by the physiotherapist^b Filled in independently by patients and physiotherapists at 26 weeks after the start of the programme^c Focus group interview with patients at the end of the study

Table 3. Characteristics of patients

	Allocated to GET	Participating in process evaluation	Not participating in process evaluation	GET completed	GET not completed	Included in focus group	No adherence to GET	GET not suitable
Number	87	78	9	73	5	9	15	7
Females (%)	51	50	56	48	80	33	40	57
Mean age (sd) ^a	51.2 (13.15)	52.0 (13.26)	45.1 (10.95)	52.1 (12.98)	50.4 (18.56)	55.6 (9.90)	50.2 (11.52)	58.6 (15.52)
Duration of complaints > 6 months (%)	79	82	56	82	80	100	87	86
Concomitant neck problems (%)	54	55	44	58	20	56	67	14
Quick onset (%)	17	17	22	16	20	33	20	14
Prior episodes of SC (%)	66	68	67	67	80	78	80	57
Severity of main complaint (0-100) ^b (sd)	76.2 (19.18)	76.4 (18.86)	74.4 (22.97)	76.3 (18.97)	78.0 (19.24)	68.9 (13.64)	78.7 (13.02)	80.00 (11.55)
Functional limitations in daily activities (0-100) ^c (sd)	66.0 (18.06)	66.0 (18.33)	65.93 (16.48)	65.9 (18.71)	68.3 (12.87)	75.7 (14.47)	69.6 (16.38)	63.5 (24.42)
Shoulder pain (7-28) ^d (sd)	17.9 (4.43)	17.7 (4.46)	19.89 (3.86)	17.6 (4.50)	18.6 (4.16)	19.2 (4.84)	19.0 (4.31)	17.0 (4.28)
Catastrophising (1-6) ^e (sd)	2.4 (0.84)	2.5 (0.86)	1.9 (0.46)	2.4 (0.84)	2.8 (1.09)	2.2 (0.72)	2.4 (0.9)	2.6 (1.01)
Coping with pain (1-6) ^e (sd)	3.0 (0.97)	3.0 (0.94)	3.5 (1.10)	3.0 (0.95)	3.1 (0.92)	2.5 (0.98)	2.9 (0.9)	2.5 (0.88)
Internal locus of control (1-6) ^e (sd)	3.3 (0.94)	3.3 (0.94)	3.2 (1.04)	3.3 (0.95)	3.4 (0.79)	3.4 (0.93)	3.2 (0.87)	3.0 (1.13)
External locus of control (1-6) ^e (sd)	2.9 (0.84)	2.9 (0.81)	2.7 (1.11)	2.9 (0.84)	2.7 (0.38)	2.7 (0.64)	3.0 (0.86)	2.9 (0.53)
Treatment preferences (yes/unclear/no) (%)								
- GET	6/88/ 6	6/88/ 6	0/100/ 0	7/86/ 7	0/100/ 0	0/89/ 11	0/93/ 7	0/100/ 0
- physiotherapy	56/38/ 6	56/38/ 6	56/44/ 0	60/33/ 7	0/100/ 0	33/22/ 45	54/33/13	43/57/ 0
- manual therapy	13/80/ 7	13/80/ 7	13/74/ 13	14/80/ 6	0/80/ 20	11/78/ 11	7/13/ 80	0/100/ 0
- analgetics	4/29/ 67	5/27/ 68	0/44/ 56	4/27/ 69	20/20/ 60	0/11/ 89	6/27/ 67	0/71/ 29
- NSAIDs	7/36/ 57	7/33/ 60	11/55/ 33	5/33/ 62	20/40/ 40	0/11/ 89	7/7/ 86	0/43/ 57
- injection	3/26/ 71	4/23/ 73	0/44/ 56	3/25/ 72	20/0/ 80	0/11/ 89	0/20/ 80	0/43/ 57
- surgery	2/22/ 76	3/21/ 76	0/67/ 33	2/22/ 76	20/0/ 80	0/0/ 100	7/60/ 33	0/29/ 71

^a standard deviation^b 11-point Likert Scale^c Shoulder Disability Questionnaire (van der Heijden et al 2000)^d Shoulder Pain Score (Winters et al 1996)^e Pain Coping and Cognition List (Berg et al 2001)

Outcome measures

Application of the programme according to protocol

Results on application of the programme are presented in table 4 and table 5. Table 4 shows numbers of sessions and the duration of the programme, listed per PT practice. The mean number of sessions and mean duration of the programme for all patients who completed the programme were 17.2 and 12.8 weeks respectively. The number of patients allocated and treated per PT practice ranged from two to 14.

Table 4. Numbers of sessions, duration of programme, allocated patients per PT practice

PT practice	Number of patients	Number of sessions ^a (sd) ^b	Duration of programme ^a (sd) ^b	Females (%)	Mean age (sd) ^b
1	8	18.0 (0.00)	15.0 (3.46)	37	54.9 (8.10)
2	9	17.8 (0.44)	13.4 (2.51)	33	48.2 (12.8)
3	8	17.3 (1.50)	14.9 (2.85)	75	44.9 (10.04)
4	2	14.0 (5.66)	9.5 (0.71)	50	38.5 (3.54)
5	13	18.0 (0.00)	12.6 (2.84)	69	49.0 (14.04)
6	8	15.6 (2.97)	11.0 (1.51)	50	60.5 (13.43)
7	7	17.3 (1.16)	9.7 (0.58)	57	51.4 (11.40)
8	10	16.0 (3.42)	13.6 (4.50)	60	57.5 (12.51)
9	8	17.7 (0.82)	12.8 (1.17)	37	45.0 (16.26)
10	14	17.4 (2.22)	12.1 (2.99)	36	52.4 (13.57)
Overall	87	17.2 (2.08)	12.8 (3.03)	51	51.2 (13.15)
Per protocol		18	12		

^a number of sessions and duration of programme in weeks

^b standard deviation

Analysis of treatment registration forms A showed that for all patients, treatment goals had been defined and agreed upon at the start of the programme, quota of activities had been set, and graphs or tables had been used during the treatment period to evaluate the progress of activities and reinforce patient behaviour.

Analysis of median scores on evaluation forms B and C showed that most physiotherapists and most patients were strongly or fully convinced that the main elements of the programme had been applied (table 5). Patients were in general more certain about the degree of application of the main elements of the programme than physiotherapists. Both physiotherapist and patients were very certain that pain-related disability had been reviewed at the start of the programme (92%). They gave equal ratings for the reconceptualisation of barriers and obstacles towards recovery at the start of the programme (78%) and 81% of both groups were strongly or fully convinced that graded activity principles were applied during the treatment period. Physiotherapists were less certain about the process of goal setting (59%) and the application of time contingency principles (60%) than patients (85% and 82% respectively). Both physiotherapists (86%) and patients (78%) reported that the emphasis of reinforcement during treatment had been on pain-related disability. Patients were less certain that management of new goals had been reviewed as part of the generalisation process (62%).

Table 5. Main elements, adherence and suitability

	Evaluation forms PTs (B)				Evaluation forms patients (C)			
1. Application of programme according to protocol								
1.3 Main elements of treatment N=73								
Scores	1 - 2 ^a	3 ^b	4 - 5 ^c	Median ^d	1 - 2 ^a	3 ^b	4 - 5 ^c	Median ^d
Reconceptualisation								
Pain-related disability	67	6	0	1 ^d	67 ^e	6		1 ^d
N (%)	(92)	(8)	(0)	(1-2) ^e	(92) ^f	(8)	(0)	(1-2) ^e
Pain beliefs	49	18	6	2	58	10	5	1
	(67)	(25)	(8)	(1-3)	(79)	(14)	(7)	(1-2)
Social factors	62	11	0	2	57	11	5	1
	(85)	(15)	(0)	(1-2)	(78)	(15)	(7)	(1-2)
Main complaint	53	17	3	2	64	6	3	1
	(73)	(23)	(4)	(1-3)	(88)	(8)	(4)	(1-2)
Barriers and obstacles	57	10	6	2	57	10	6	2
	(78)	(14)	(8)	(1-2)	(78)	(14)	(8)	(1-2)
Goal-setting	43	18	12	2	62	8	3	1
	(59)	(25)	(16)	(1-3)	(85)	(11)	(4)	(1-2)
Graded activity	59	12	2	2	59	9	5	2
	(81)	(16)	(3)	(1-2)	(81)	(12)	(7)	(1-2)
Time contingency	44	13	16	2	60	8	5	2
	(60)	(18)	(22)	(1-3)	(82)	(11)	(6)	(1-2)
Operant conditioning								
Pain behaviours	51	11	11	2	49	9	15	2
	(70)	(15)	(15)	(1-3)	(67)	(12)	(21)	(1-3)
Pain-related activities	63	10		2	57	3	13	2
	(86)	(14)	(0)	(1-2)	(78)	(4)	(18)	(1-2)
Generalisation								
Self-management	59	10	4	2	61	8	4	1
	(81)	(14)	(5)	(1-2)	(84)	(11)	(5)	(1-2)
New goals	50	13	10	2	45	21	7	2
	(68)	(18)	(14)	(1-3)	(62)	(29)	(9)	(1-3)
Application of treatment	52	13	8	2	54	6	13	2
Principles after treatment	(71)	(18)	(11)	(1-3)	(74)	(8)	(18)	(1-3)
2. Adherence to the programme N=77								
	59	7	11	2	55	7	15	2
	(77)	(9)	(14)	(1-2)	(71)	(9)	(20)	(1-3)
3. Suitability of the programme N=77								
	53	8	16	2	62	8	7	1
	(69)	(10)	(21)	(1-3)	(81)	(10)	(9)	(1-2)

^a Score 1-2 = fully or strongly convinced^b Score 3 = reasonably convinced^c Score 4-5 = little or not at all convinced^d Median^e Percentiles (25-75)

Patients who participated in the focus group interview mentioned that the rationale of the programme had been appropriately explained at the start of the programme. Eight of the nine participants confirmed that the items listed under the heading of 'reconceptualisation' had been reviewed, mainly in the first session.

Participants to the focus group interview mentioned that clear treatment goals related to daily activities had been defined and agreed upon at the start of the programme. However, five of them had experienced difficulties in setting treatment goals and reported that their aims had been strongly influenced by the physiotherapists' experience. Two patients reported that goals had been adjusted several times during the treatment period. For one patient, these adjustments had been made because of lack of progress, while for the other patient it had been because of successful progress.

All participants in the focus group confirmed consistent application of graded activity and time-contingent principles during the treatment period and reported clear advantages of the systematic approach to their complaints. Four participants, however, had also experienced difficulties in the performance of time-contingent exercises during the treatment, especially in situations of unsatisfactory progress and conflicting recommendations by health care providers. Participants reported that the items relating to generalisation had not always been reviewed in detail, but there was an ongoing process of applying what they had learned in everyday life.

Patient adherence

Analysis of evaluation forms B and C showed that 77% of the physiotherapists and 71% of the patients were fully or strongly convinced that patients had satisfactorily adhered to the programme (table 5), indicating that physiotherapists were more confident about the way patients had participated in the programme than patients were confident of their own participation. Characteristics of patients who were not confident of their adherence were comparable to those of all patients allocated to GET (table 3).

Participants of the focus group interview were all confident about their adherence to the programme. They mainly attributed their adherence to the efforts they had made to attain preset levels of daily activities.

Suitability of the programme

Sixty-nine percent of the physiotherapists and 81% of the patients were fully or strongly convinced that the programme was suitable for SC patients (table 5). Physiotherapists rated the programme as unsuitable for 21% of the patients, and 9% of the patients considered the programme to be unsuitable for their own SC. Table 3 shows that patients who considered the programme to be unsuitable had less concomitant neck problems and were comparable to other patients allocated to GET in terms of their other characteristics.

Seven patients participating in the focus group interview assessed GET as a suitable treatment for their own complaints, irrespective of the outcomes in terms of effectiveness. One patient was doubtful about the suitability for her own complaints because her levels of activities had not increased as expected. One patient was doubtful because she had experienced more complaints and had ended the programme after eight sessions. All patients reported they would recommend the programme to other patients suffering from SC.

DISCUSSION AND CONCLUSION*Discussion*

Process evaluation is of utmost importance in studies on clinical effectiveness: first, to know whether the treatment under study was performed according to protocol, second, to know whether the treatment is feasible in normal practice, and third, to identify needs for improvement of the protocol to facilitate implication. However, still little attention is paid to process evaluation in trials. Possible explanations for a lack of information on the intervention process were reported earlier by van Haastregt et al (van Haastregt et al 2002). Firstly, there is a lack of measurement instruments for evaluating intervention processes and these evaluations are mostly time-consuming. Secondly, only little attention is paid to detailed description of the intervention process in trials in the most recent version of the CONSORT statement (Consolidated Standards of Reporting Trials). Thirdly, since researchers and publishers pay most attention to publication of clinical results of a trial, information on the intervention process often remains unpublished. We recommend developing of measurement instruments for evaluating intervention processes and reporting on process evaluations in trials and on implications for clinical effectiveness and for clinical practice.

The present process evaluation was embedded in our study on clinical effectiveness of GET in patients with chronic SC. We reported on the application of the programme, its perceived suitability and on patient's adherence. We mainly focused on quality assurance of treatment outcomes at this stage of the evaluation and suggest that more detailed qualitative assessment on satisfaction with the programme has to be performed if it shows to be effective.

We conclude that in this trial, the GET programme was applied according to the protocol to an acceptable extent and that the programme is feasible in normal practice, as participants in the focus group interview confirmed. First, the number of sessions (17.2) and duration of the programme (12.8 weeks) were applied according to the protocol to an acceptable extent. These findings are comparable to the completion rate of scheduled exercise sessions in an other recently performed study on the effectiveness of an exercise programme for shoulder disorders (McNeely et al 2004). Second, with regard to the application of main elements of the programme, results show that 75% of the physiotherapists and 79% of the patients who completed the programme were strongly or fully convinced that these were applied. We found that 85% of the physiotherapists and 84% of the patients were fully or strongly convinced that the main elements pertinent to pain-related disability had been applied (reconceptualisation of pain-related activities, gradually rising levels of pain-related activities, reinforcement on pain-related activities and self-management of complaints). Given the aim of the programme to increase levels of daily activities, we consider these items to be very important in our evaluation of the intervention process. Third, with regard to patient adherence to the programme: 77% of the physiotherapists and 71% of all patients were confident of the way the patients had participated in the programme. These findings were very much similar to adherence rates reported in other recently performed studies on effectiveness of exercise programmes (Messier et al 2004, Lin et al 2004, van Santen et al 2002, Wullink 2001). Given that this was a pragmatic trial, an adherence rate of more than 70% reasonably allows the conclusion that patient adherence to the programme was as expected. Fourth, with regard to the suitability of the programme: 69% of the physiotherapists and 81% of the patients was fully or strongly convinced that the programme was indeed suitable for the participants. Physiotherapist rated the programme as unsuitable for 21% of the

included patients, while 9% of the patients rated the programme as unsuitable. All participants in the focus group interview would recommend the programme to other patients with SC, irrespective of the effectiveness experienced at the time of the interview. However, two participants in the focus group interview considered the programme unsuitable for their own complaints due to unsuccessful progress or to more complaints. Patients who considered the programme unsuitable (N=7), reported less concomitant neck problems, but since numbers are small, we suggest that these findings on perceived suitability have to be linked with outcomes on clinical effectiveness, before recommendations on suitability for (subgroups of) patients with SC can be given.

Two elements need further attention in the implementation of GET: the process of goal-setting and management of new goals after treatment, and the application of time-contingent principles. Reports showed that treatment goals were indeed set for all participants, however, physiotherapists were little or not at all convinced of the application of goal-setting as planned in 16% of the patients, and participants in the focus interview reported difficulties in defining achievable treatment goals and management of new goals after treatment. An earlier study on this topic showed that only 32% of patients selected exactly the same three main complaints from a list of 36 activities during the first and second intake visits in a study on low back pain (Beurskens et al 1999). The GET programme could therefore be improved by reviewing treatment goals more than once during the start-up period and by emphasising and evaluating the management of (new) goals more often during the treatment period. In 22% of all patients, the physiotherapists were little or not at all convinced of the application of time contingency principles as planned. Patients in the focus group mentioned difficulties with this item in situations of unsatisfactory progress and conflicting recommendations by other health care providers, such as the general practitioner. Application of the principles of time contingency seems to be more difficult in a primary care setting if the approach of other health care providers (e.g. general practitioners) is based on pain contingency principles. Implementation in regular practice could be facilitated if the principles of graded exercise are embedded in a multi-disciplinary approach and reinforcement of patients' pain behaviours is uniform. Physiotherapists should be aware of these difficulties with application in clinical practice.

In the present process evaluation, there are some methodological weaknesses. First, since indirect methods were used, we can only present reports, and have no evidence of what actually happened. Second, since providers are involved in the assessments, scores might be flawed (higher). Third, reports on the quantitative application of the programme do not provide information about the quality of its application. Fourth, these data might be affected by the physiotherapists' and patients' perception of the improvement on the complaints. Fifth, adherence and suitability in this study were assessed by single items only. In order to avoid bias and to overcome interference of the assessment with the treatment process, data were taken from physiotherapists and patients independently and in concealment after the treatment period was ended. However, we suggest that validity of these evaluations could be improved by additional assessments of treatment sessions by an independent observer and by using more detailed and standardised measurement instruments.

Conclusion

Process evaluation of a clinical study is essential to interpret the extent of clinical effectiveness as is shown in this trial on the GET programme. We expect that the effectiveness of the programme as applied in the trial will not be influenced by flaws in its application or by lack

of patient adherence. The programme was considered suitable for 79 to 91 percent of the participants in this trial.

Practice implications.

Process evaluation gives indication for improvement. In the case of the GET it could be improved in terms of the process of goal-setting, and the implementation of the GET programme could be facilitated if the programme is embedded in a multidisciplinary approach in primary care. We suggest that more detailed qualitative assessment on satisfaction with the programme and on optimising the treatment is needed, if it proves to be effective.

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CHAPTER 7

Comparison of two recruitment strategies for patients with chronic shoulder complaints

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Comparison of two recruitment strategies for patients with chronic shoulder complaints

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ABSTRACT

Background: Recruiting adequate numbers of participants represents a major problem to the completion of randomised clinical trials in primary care. Information on different recruitment strategies applied in one trial is scarce.

Aim: To evaluate the application of two recruitment strategies in one trial.

Design of study: The study was performed within the framework of a randomised clinical trial on the effectiveness of a behavioural treatment for patients with chronic shoulder complaints.

Setting: Thirty-two general practices in the Netherlands.

Methods: Patients recruited during a consultation with their general practitioner (GP) for chronic shoulder complaints were compared with patients recruited by advertisement in a local newspaper as regards baseline characteristics, withdrawals (drop-outs and losses to follow-up) and post-treatment clinical outcomes.

Results: Patients recruited by the general practitioners (N=83) were similar to those recruited by advertisement (N=93) in terms of demographic characteristics and clinical outcome measures at baseline, but differed slightly in disease characteristics and treatment preferences. Recruitment strategy was not related to reasons for or numbers of withdrawals. Improvements on outcome measures were greater in patients recruited by the general practitioners, irrespective of allocated treatment. Results on the clinical effectiveness of treatments at the end of the treatment period or during follow-up were neither modified by recruitment strategy, nor

by differences between the two strategy groups in patient characteristics found at baseline.

Conclusion: Using two recruitment strategies did not influence the outcomes on clinical effectiveness in this trial. However, recruitment strategy should be considered as a putative modifying factor in the design of a study.

Key words: patient selection, family practice, randomised clinical trial, behavioural therapy, shoulder.

INTRODUCTION

Recruiting adequate numbers of participants currently represents a major problem to the completion of randomised clinical trials, in particular in primary care (Foy et al 2003). Several studies on recruitment in primary care have been done so far, mainly focusing on preventing and overcoming recruitment problems before starting a study. Common outcome measures in these studies are numbers of referrals and recruitment rates.

Several studies have reported on characteristics of patients, the general public or general practitioners (GP) and on methodological options to overcome recruitment problems in primary care settings. Willingness to participate and attendance among patients seem to be associated with demographic factors (age, gender, marital status, social class, occupation, education), attitudes (readiness to change), and disease characteristics (clinical measures, health status, risk factor status) (Boles et al 2000, Damush et al 2002, Lloyd-Williams et al 2003, Nazemi et al 2001, Saunders et al 2000, Thorogood et al 1993, Trauth et al 2000). In general, demographic characteristics and attitudes seem to be better predictors of recruitment rates and attendance than disease characteristics. Treatment preferences of participants might influence the outcome in non-blinded studies (van Schaik et al 2004, Thomas et al 2004, van der Windt et al 2000). Patient recruitment by general practitioners seems largely determined by the general practitioners' motivation, involvement, forgetfulness, time pressure and financial reimbursement (Gurwitz et al 2001, Pearl et al 2003, Peto et al 1993, de Wit et al 2001). Methods and strategy of recruitment, e.g. screening by a general practitioner, waiting room screening, or recruitment by advertisements, seem to be related to the yield in numbers of qualified patients and the costs per recruited patient (de Wit et al 2001, Davey et al 2003). Organisational characteristics and the simplicity of printed information for the patients and general practitioners seem to influence recruitment rates as well (Foy et al 2003, Bell-Seyer and Moffet 2000, Prout et al 2003).

One question, which has not been answered so far, is what should be done if, despite all efforts, the recruitment stage delays or hampers the proper conduct of a trial. The present study evaluated the application of two recruitment strategies in one trial examining the effectiveness of a behavioural treatment for patients with chronic shoulder complaints. Since the numbers of patients recruited during general practitioner consultations were smaller than expected, subjects were also invited to enrol by means of advertisements in a local newspaper. Since patient inclusion and exclusion criteria were similar for both strategies, one might assume that the characteristics of patients enrolled by both strategies would be comparable and that the recruitment method would not influence the course and outcomes of the trial. To evaluate this assumption, we compared the effects of these two strategies with respect to baseline characteristics, withdrawals (drop-outs and losses to follow-up) and post-treatment outcomes.

METHODS

Design

This study was performed within the framework of a trial on the effectiveness of a behavioural Graded Exercise Therapy programme for patients with chronic shoulder complaints. The programme aims to improve performance of daily activities and healthy behaviours and to reduce health care utilisation during the treatment period and the one-year follow-up period. More details of the design and the results of this trial have been presented elsewhere (Geraets et al 2004, Geraets et al 2005).

Two strategies were used to enrol patients in this trial: recruitment by general practitioners during consultations for shoulder complaints (from January 2002 until July 2003) and recruitment by advertisement in a local newspaper (from March 2003 until July 2003). We used block randomisation, with blocks of 10 patients, to allocate participants either to Graded Exercise Therapy or to usual care. To compare the effects of the two recruitment strategies, we assessed patient characteristics at baseline, number of withdrawals (drop-out rate and losses to follow-up), reasons to withdraw, and the influence on primary outcome measures (main complaint instrument and Shoulder Disability Questionnaire) at the end of the treatment period (12 weeks) and during follow-up (26 and 52 weeks).

Participants

Patients with shoulder complaints for at least three months, at least 18 years old, and living in the Province of Limburg (the Netherlands), were invited to participate in the study.

Recruitment strategies

Recruitment during consultation in general practice

Forty-nine general practitioners working in the area of the twenty physiotherapists involved in the study, were invited to participate. Thirty-two general practitioners agreed to participate and recruited patients who visited their surgery and met the selection criteria. A research assistant visited potential participants at home within two weeks after the general practitioner had seen them.

Recruitment by advertisement in a local newspaper

An advertisement in a local newspaper (circulation rate 159.000 addressees) was used to enrol patients. After the research assistant had checked their eligibility by telephone, patients received written information about the content of the study. The research assistant then contacted the patient's general practitioner. If the general practitioner was not able or did not want to check the selection criteria, an independent general practitioner associated with the trial team checked these. If patients met the selection criteria, a research assistant visited them at home within two weeks.

Outcome measures

Baseline characteristics

Demographic variables, disease characteristics, putative prognostic factors, treatment preferences and outcome variables of clinical effectiveness were determined at baseline.

Drop-out rate and loss to follow-up

Drop-out rates during treatment and losses to follow-up were assessed. We also determined reasons to withdraw for both strategies in relation to allocated treatment.

Outcomes after treatment and during follow-up

Differences between the two recruitment strategy groups in terms of clinical outcome measures were established for both treatments at 12, 26 and 52 weeks. We assessed the influence of the recruitment strategy and possible confounders or modifying factors on the primary outcome measures of clinical effectiveness of treatments.

Statistical analysis

Analyses were carried out with SPSS statistical software (version 12.0) according to the intention-to-treat principle. A p-value of <0.01 was considered to be statistically significant (two-tailed) for all comparisons.

First, the sample size was calculated based on figures of perceived recovery (van der Windt et al 1996). Since we aimed to increase the recovery rate from 25% to 50%, at a 1-sided alpha of 5%, a statistical power (1-beta) of 0.90, and a 10% dropout rate, we needed 66 persons per treatment group.

Subsequently, the standardized difference (the ratio of the differences between groups to the standard deviation of the observations) was determined according to the sample size of the trial as a measure of the expected differences in outcome post treatment (Altman 1991). The standardized difference was determined to be 0.52. The differences between recruitment groups on clinical outcome measures at baseline were considered with respect to the determined standardized difference to evaluate the influence of recruitment strategy at baseline.

Then, effect sizes (the ratio of the differences in mean change scores to the standard deviation of the average change scores of the total population) were calculated to evaluate the differences between recruitment groups on clinical outcome measures after treatment and during follow-up. Effect-sizes of 0.2, 0.5, and 0.8 were considered as small, medium and large beneficial effects respectively (Cohen 1977). Confidence intervals (95%) of the mean differences were determined and analysed by Student's T-tests for data with a Gaussian distribution, and by Mann-Whitney tests for non-Gaussian distributions. Furthermore, we analysed the differences between the recruitment groups for both treatments.

Finally, the influence of recruitment strategy and possible confounding or modifying factors which differ between recruitment groups at baseline on the primary outcome measures, was analysed using multivariate linear regression and a stepwise forward procedure ($p < 0.10$). Covariates that were significantly associated with the primary outcome measure after the variable 'treatment' was included in the model, remained in the final model and were considered as confounders. If the interaction term (the product of the covariate and 'treatment') was significantly associated as well, the covariate was considered as a modifying factor. Adjusted estimates were reported in case of confounding or effect modification.

RESULTS

Ninety patients were recruited by the general practitioners during consultations (figure 1). Seven of these patients (8%) were excluded before randomisation (for reasons, see figure 1). One-hundred-and-two patients recruited by advertisement were eligible to participate according to their general practitioners. Nine of these patients (9%) were excluded before randomisation. A total of 176 patients were randomised and allocated to either Graded Exercise Therapy ($N=87$) or usual care ($N=89$).

Table 1 shows that the two recruitment groups were comparable on most demographic variables and all clinical outcome variables at baseline. Patients recruited by advertisement had a higher average educational level. Duration of complaints was longer for these patients, whereas periods of sick leave were shorter.

Figure 1 shows that reasons to withdraw from the study, drop-out rates, and losses to follow-up at 52 weeks were similar for both recruitment strategy groups (16% for general practitioner recruitment versus 17% for recruitment by advertisement).

Figure 1. Flow-chart¹

¹ Number between brackets is number of patients

² GET=Graded Exercise Therapy

³ UC=usual care

Patients recruited by advertisement were slightly less ambivalent in their preferences for commonly applied shoulder complaints treatments and prior treatments had been less successful in these patients (table 2).

Table 3 shows that mean improvements among patients recruited by the general practitioners were statistically significantly greater for the main complaints instrument at 52 weeks ($p=0.001$; effect-size 0.50) and for the Shoulder Disability Questionnaire at 26 weeks ($p=0.005$; effect-size 0.43) and 52 weeks ($p=0.004$; effect-size 0.44).

Table 1. Baseline characteristics

	Recruited by the GPs	Recruited by advertisement
Number	83	93
Demographic variables		
Age (years) (sd)	52 (12.4)	52 (12.6)
Females (%)	54	55
Employed (%)	58	56
Education (low) (%)	77	67
Specific disease variables		
Duration of shoulder pain (> 6 months) (%)	69	87
Sick leave (if employed) in past 8 weeks (> 1 week) (%)	15	2
Concomitant neck problems (%)	46	48
Prior episodes of shoulder complaints of at least 1 week in past year (>5) (%)	70	68
Primary outcome measures		
Performance of daily activities:	75.3 (18.30)	72.9 (20.51)
Severity of main complaints (0-100)	66.9 (18.36)	64.9 (19.49)
Functional limitations to daily activities (SDQ) (0-100)		
Secondary outcome measures		
Shoulder pain (SPS) (7-28)	17.3 (4.11)	17.6 (4.22)
Pain intensity (11-point scale) (0-10)	5.5 (1.98)	5.6 (2.00)
Quality of life (EuroQol-5D) (-1 to 1)	0.67 (0.224)	0.67 (0.212)
Kinesiophobia (2 items TSK) (1-7)	2.9 (1.99)	2.7 (1.94)
Fear-Avoidance Beliefs (5 item subscale FABQ) (1-7)	4.3 (1.37)	4.5 (1.20)
Catastrophising (12 item subscale PCCL) (1-6) ¹	2.3 (0.82)	2.4 (0.82)
Coping with Pain (11 item subscale PCCL) (1-6) ¹	3.0 (1.02)	3.1 (0.83)
Internal locus of control (11 item subscale PCCL) (1-6) ¹	3.5 (0.93)	3.4 (0.89)
External locus of control (7 item subscale PCCL) (1-6) ¹	3.0 (0.88)	2.9 (0.81)

¹ PCCL subscale scores: very low (1.0-1.9), low (2.0-3.4), high (3.5-5.0), very high (5.1-6.0)

Table 4 shows that patients recruited by the general practitioners showed greater improvement on both primary outcome measures, irrespective of treatment allocation.

Multivariate linear regression analyses (table 5) shows that recruitment strategy was significantly associated with both primary outcome measures (the main complaint instrument at 52 weeks and the Shoulder Disability Questionnaire at 26 and 52 weeks). This indicates that recruitment strategy was a confounding factor. There was no interaction between Graded Exercise Therapy and recruitment strategy (the interaction term of recruitment and 'treatment' failed to reach significance and was excluded from all models). The lack of interaction indicates that the clinical effectiveness of the programme, as assessed by the primary outcome measures at the end of treatment and during follow-up, was not modified by the recruitment strategy. Other possible modifiers (educational level, duration of pain, duration of limitations, sick leave or treatment preferences) were not significantly associated with these clinical outcome measures and were excluded from all models.

Table 2. Treatment experiences and preferences

Treatment:	Experienced success-rate of treatment ¹		Treatment preference ²	
	GP (%)	Advertisement (%)	GP (no/unclear/yes)(%)	Advertisement (no/unclear/yes)(%)
• Behavioural therapy	-	10	2 / 90 / 8	15 / 73 / 12
• Physiotherapy	47	27	10 / 34 / 46	11 / 38 / 51
• Manual Therapy	64	31	10 / 77 / 13	18 / 61 / 21
• Analgesics	59	48	69 / 26 / 5	77 / 16 / 7
• NSAIDS	60	48	66 / 30 / 4	65 / 26 / 9
• Corticosteroid injection	47	42	68 / 29 / 3	78 / 18 / 4
• Surgery	64	39	79 / 20 / 1	81 / 16 / 3

¹ Patients who had prior experiences with common treatments for shoulder complaints were asked whether they had experienced these treatments as successful

² Patients were asked to rate their treatment preference on a 5-point scale (1-2=no; 3=unclear; 4-5=yes)

Table 3. Mean improvement for both recruitment groups on primary outcome measures after 12, 26 and 52 weeks¹

	GP N=83	Advertisement N=93		Differences between groups			
	Mean (sd)	Mean (sd)	Mean diff	95% CI of diff ²		P-value ³	Effect size
Main complaints (0-100)							
12 weeks	32.3 (25.7)	26.0 (24.7)	6.3	-1.2	13.8	0.098	0.25
26 weeks	39.1 (28.2)	30.9 (26.5)	8.2	0.0	16.3	0.049	0.30
52 weeks	43.4 (28.5)	30.1 (24.8)	13.3	5.3	21.2	0.001	0.50
SDQ (0-100)							
12 weeks	20.9 (23.9)	12.0 (23.0)	8.9	1.9	15.9	0.013	0.38
26 weeks	27.7 (28.8)	15.7 (26.8)	12.0	3.7	20.3	0.005	0.43
52 weeks	27.9 (29.4)	15.6 (27.1)	12.3	3.9	20.7	0.004	0.44

¹ After unconditional mean imputation

² 95% confidence interval of difference

³ Statistically significant P<0.01

DISCUSSION AND CONCLUSIONS

Summary of main findings

Patients recruited for a randomised clinical trial by general practitioners and by advertisement were comparable in terms of most baseline characteristics and numbers of withdrawals (drop-outs and losses to follow-up). Patients recruited by the general

Table 4. Mean improvement for both recruitment groups and both intervention groups on primary outcome measures after 12, 26 and 52 weeks¹

Mean improvement on primary outcome measures for Graded Exercise Therapy							
	GP N=41	Advertisement N=46		Differences between groups			
	Mean (sd)	Mean (sd)	Mean diff	95% CI of diff ²		P-value ³	Effect size
				lower	upper		
Main complaints (0-100)							
12 weeks	35.8 (28.3)	30.0 (23.0)	5.8	-5.1	16.8	0.294	0.23
26 weeks	43.6 (27.9)	33.7 (25.0)	9.9	-1.4	21.1	0.085	0.37
52 weeks	49.1 (28.1)	33.9 (23.3)	15.3	4.3	26.2	0.007	0.60
SDQ (0-100)							
12 weeks	22.2 (26.1)	12.4 (25.3)	9.9	-1.1	20.8	0.077	0.39
26 weeks	27.2 (28.1)	18.5 (29.5)	8.7	-3.6	21.0	0.162	0.30
52 weeks	27.1 (26.2)	18.3 (25.9)	8.8	-2.3	19.9	0.120	0.34
Mean improvement on primary outcome measures for Usual Care							
	GP N=42	Advertisement N=47		Differences between groups			
	Mean (sd)	Mean (sd)	Mean diff	95% CI of diff ²		P-value ³	Effect size
				lower	upper		
Main complaints (0-100)							
12 weeks	28.9 (22.7)	22.1 (25.9)	6.8	-3.5	17.1	0.192	0.28
26 weeks	34.7 (28.0)	28.2 (28.0)	6.5	-5.3	18.4	0.274	0.23
52 weeks	37.8 (28.1)	26.5 (25.9)	11.4	-0.3	22.7	0.051	0.42
SDQ (0-100)							
12 weeks	19.6 (22.0)	11.6 (20.7)	8.0	-1.0	17.0	0.080	0.37
26 weeks	28.3 (29.8)	13.1 (24.0)	15.2	3.9	26.6	0.009	0.57
52 weeks	28.7 (32.5)	13.0 (28.2)	15.7	2.9	28.5	0.017	0.52

¹ After unconditional mean imputation² 95% confidence interval of difference³ Statistically significant $P < 0.01$

practitioners showed greater improvement on both primary outcome measures, irrespective of treatment allocation. Multivariate regression analyses showed that clinical effectiveness at the end of the treatment or during follow-up was not modified by the recruitment strategy, or by baseline differences between the two recruitment strategy groups.

Strengths and the limitations of this study

Our results show that findings on effectiveness in the trial are applicable to both patients who consulted their general practitioners for their complaints and patients who did not intend to visit their general practitioners. However, the use of two recruitment strategies did introduce a confounding factor. Although multivariate regression analyses showed that the recruitment strategy did not modify the outcome of the trial in terms of effectiveness, we found that mean

Table 5. Adjusted analyses on primary outcome measures ¹

Model ²	Variables	Coefficient B ³	95% CI of diff ⁴		P-value ⁵
			lower	upper	
Main complaints; mean differences between groups (0-100)					
Model 12.1	Included: GET	7.5	0.0	15.0	0.049
	Excluded: Recruitment strategy				0.095
Model 26.1	Included: GET	7.1	-1.0	15.2	0.084
	Excluded: Recruitment strategy				0.047
Model 52.1	Included: GET	9.2	1.4	17.1	0.021
	Recruitment strategy	-13.3	-21.1	-5.5	0.001
	Excluded:				
	GET * Recruitment Strategy				0.624
SDQ; mean differences between groups (0-100)					
Model 12.2	Included: GET	1.7	-5.3	8.7	0.636
	Excluded: Recruitment strategy				0.013
Model 26.2	Included: GET	2.3	-5.9	10.6	0.578
	Recruitment strategy	-12.0	-20.3	-3.7	0.005
	Excluded:				
	GET * Recruitment Strategy				0.441
Model 52.2	Included: GET	2.1	-6.3	10.5	0.624
	Recruitment strategy	-12.3	-20.7	-3.9	0.004
	Excluded:				
	GET * Recruitment Strategy				0.418

¹ After imputation of the overall mean² Adjusted analyses of the main complaint instrument (model 12.1, 26.1, 52.1) and SDQ (model 12.2, 26.2, 52.2) after 12 weeks of treatment and during follow up at 26 and 52 weeks respectively³ Regression coefficient for GET (GET=1; UC=0) and for recruitment strategy (Advertisement=1; GP=0).⁴ 95% confidence interval of difference⁵ Statistically significant P<0.01

improvements among patients recruited by the general practitioners were greater, irrespective of treatment allocation. In our trial, clinical effectiveness was not influenced, because patients recruited by the general practitioners and by advertisement, were allocated by block randomisation and equally balanced for both treatment groups. If this had not been the case, outcomes could have been biased. For example, small differential effects between recruitment

groups would have been more pronounced if 75% of patients had come from advertisement and 25% from the general practitioner.

Patients recruited by the general practitioners and those enrolled by advertisement turned out to be only slightly dissimilar with respect to level of education, duration of complaints, sick leave and treatment preferences. Sick leave among patients recruited by the general practitioners during consultations was longer, which suggests that sick leave might be a reason for patients to visit their general practitioners because of shoulder complaints. Since blinding was not feasible at the patient or provider level, treatment preferences may have influenced outcome measures of effectiveness (Thomas et al 2004, van der Windt et al 2000). However, multivariate linear regression showed that these possible modifiers did not alter the results on clinical effectiveness.

Patients recruited by the general practitioners showed greater mean improvements on the primary outcome measures than those recruited by advertisement, irrespective of treatment allocation. Effect-sizes between recruitment groups reached up to the level of the expected difference in outcome post treatment (0.50). We were unable to explain these findings by possible confounders or modifying factors in our dataset.

Comparison with existing literature

Several studies on the effectiveness of cognitive behavioural treatment have reported on influences of pre-treatment attitudes (readiness to change, motivation) and beliefs (expectancies) on pain and pain disability (Dijkstra et al 2001, de Gier et al 2004, Goossens et al 2004, Jensen et al 2003, Jensen et al 2004, Keefe et al 2004, Lackner et al 1996). These studies showed that pain-catastrophising, pain anxiety, pain-related fear, helplessness and unsuccessful prior treatment experiences seem to be associated with over-predicting actual pain and under-predicting abilities to perform physical tasks and to adjust pain behaviour, and these patients have low treatment expectancies. By contrast, self-efficacy, better pain coping and control, pain acceptance and readiness to change seem to be associated with decreased pain, improved physical performance and better adjustment to pain. Those patients probably have higher treatment expectancies.

Since the primary outcome measures in our trial were subjective, we assume that pre-treatment attitudes and beliefs may also have influenced the prognosis of patients in this study. We considered the possibility that pre-treatment expectancies and readiness to change in patients recruited by the two strategies in this trial may have been dissimilar. To begin with, patients recruited by the general practitioners had decided to visit their general practitioners for their complaints, whereas patients recruited by advertisement did not intend to contact their general practitioners. Patients recruited by the general practitioners were asked to participate, whereas those recruited by advertisement reacted spontaneously to an announcement in a local newspaper. Furthermore, we found that patients recruited by the general practitioners had had more successful experiences with all treatments commonly applied for shoulder complaints. As a result, their expectations about shoulder treatments in general may have been higher, whereas expectations among patients recruited by advertisement were probably lower as regards commonly applied treatments and probably only higher as regards the new behavioural programme. Unfortunately, detailed information on these attitudes and beliefs, as possible prognostic factors, was not available in our dataset.

Eighty-three patients were enrolled by the general practitioners over a period of fourteen months, whereas 93 patients were recruited by advertisement over a period of four months.

In terms of efficiency, the recruitment rate for advertisements was thus considerably higher. These findings confirm that recruitment strategies in which the general practitioner plays an active role as gatekeeper are less efficient (Gurwitz et al 2001, Davey et al 2003).

Implications for future research

Demographic and disease characteristics are important variables with respect to recruitment rates, as has been reported above. In the present study, however, these factors did not account for differences we found in the prognosis of patients recruited by different strategies. Therefore, we recommend that more specific potential modifiers relating to recruitment strategy (e.g., beliefs and attitude) should be included in the design of studies and recruitment strategies (in addition to the above-mentioned demographic and putative disease-specific prognostic factors). We conclude that using two recruitment strategies did not influence the outcomes on clinical effectiveness of our trial. However, this conclusion is based only on analyses of our data and differential effects might be different if other groups have to be adopted. Recruitment strategy should be considered as a putative modifying factor in the design of a study and we recommend further research into this phenomenon.

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CHAPTER 8

General discussion

This thesis reports on a study evaluating the effectiveness and cost-effectiveness of a behavioural Graded Exercise Therapy programme, in comparison with usual care, for patients with chronic shoulder complaints in a primary care setting. This final chapter summarises the main findings of the randomised clinical trial and the answers to the research questions presented in the first chapter. Also methodological and practical issues, including the recruitment of patients and the intervention process, will be discussed. Finally, the implications for clinical practice will be considered and recommendations are made for future research and practice developments.

MAIN FINDINGS

In total 176 patients are recruited, either by their general practitioner (N=83) or through advertisements (N=93). Block randomisation is used (blocks of ten patients each) to allocate patients to Graded Exercise Therapy (GET) (N=87) or to usual care (UC) (N=89) according to the guidelines for shoulder complaints issued by the Dutch College of General Practitioners (Winters et al 1999). Two primary outcome measure are used to assess the performance of daily activities: the 'main complaints' instrument and the Shoulder Disability Questionnaire (SDQ) (Beurskens et al 1999, van der Heijden et al 2000). The experimental GET method was characterised by graded activity, time contingency and operant conditioning, while usual care consisted of information, recommendations and pain-contingent medical or pharmaceutical therapy (see chapter 2 for details).

Short-term and long-term clinical effectiveness

The first and second research questions are concerned with the short-term and long-term clinical effectiveness of GET (chapters 3 and 4). GET patients showed statistically significantly greater improvement than UC patients on the 'main complaints' instrument immediately after the 12-week treatment, and these improvements lasted for at least 52 weeks. Improvements on the SDQ were greater with GET than with UC, but the differences between the groups failed to reach statistical significance. Explorative analyses showed that GET was more effective in patients not reporting pain reduction over time and in patients showing no painful arc during physical examination. Significantly greater improvements with GET were found for catastrophising at 12 weeks and for fear-avoidance beliefs and kinesiophobia at 52 weeks.

Cost-effectiveness

The third research question is related to the cost-effectiveness of GET (chapter 5). Patients allocated to GET showed statistically significantly lower direct health care costs and direct non-health care costs during the follow-up period compared to patients allocated to UC. Nevertheless, since the costs of the GET programme were higher than those of UC, total costs for GET patients were significantly higher than for UC patients. The costs per patient to improve the performance of daily activities by 25%, which was the aim of this trial, were calculated to be € 425.

Process evaluation

The fourth research question deals with the intervention process (chapter 6). The clinical effectiveness of GET in this trial was not influenced by flaws in the application of the

programme or by lack of patient adherence. GET can be administered successfully by physiotherapists in a primary care setting. The programme could be improved in terms of the process of goal-setting, and the implementation of the GET programme could be facilitated if recommendations on pain-behaviours and pain-related disability given by health care providers in primary care are better matched.

Recruitment strategy

The final research question is related to the two recruitment strategies used in this trial (chapter 7). Results in terms of the clinical effectiveness of the treatments at the end of the treatment period or during follow-up are not modified by the recruitment strategy used. However, patients recruited by a general practitioner showed greater improvements on both primary outcome measures, irrespective of the allocated treatment. Therefore, recruitment strategy should be regarded as a putative modifying factor in the design of further studies.

METHODOLOGICAL AND PRACTICAL ISSUES

This study was a pragmatic randomised clinical trial, studying the effectiveness of the behavioural Graded Exercise Therapy programme compared with usual care in an everyday primary care setting. Opting for a pragmatic study has several methodological and practical consequences related to the design and implementation of the study. Aspects discussed below include the study population, recruitment of patients, blinding, contamination, intervention process, outcome measures and explorative analyses.

Study population

A first comment needs to be made on the selection of participants. We intended to include a representative sample of patients with chronic shoulder complaints in primary care in this trial, but as a consequence the study population was rather heterogeneous. A broad range of patients with shoulder complaints were included, and no restrictions were made for social aspects such as patients' work status. Furthermore, patients are included who visited their general practitioner for their shoulder complaints as well as those who initially did not intend to consult their general practitioner. The strength of this procedure is that the results can be easily generalised to an everyday primary care setting. However, its weakness might be an inadequate match between the GET programme and patient characteristics. As a consequence beneficial treatment effects for specific subgroups might have been underestimated.

Recruitment of patients

An other comment needs to be made about the recruitment of our patients. Because the recruitment rate of patients during general practitioner consultations turned out to be lower than expected, subjects were also invited to enrol by means of advertisements in a local newspaper. Since recruitment strategy had to be regarded as a putative confounding or modifying factor, patients were pre-stratified for recruitment strategy before block randomisation. The results showed that the number of patients allocated to GET and to UC were equally balanced between both recruitment strategies and the total numbers of patients recruited by the general practitioners and by advertisement were very similar. However, patients recruited by a general practitioner showed greater improvement in terms of both

primary outcome measures, irrespective of the allocated treatment. We learn from this study that through prestratification and randomisation the results of this trial were not biased by recruitment strategy, but the effectiveness of both treatment groups in terms of the clinical outcome measures used in this study has been underestimated.

One might argue that patients who intended to visit their general practitioner had more severe complaints, a longer duration of complaints or other treatment preferences. However, these factors did not modify the results of the trial, so no explanation was available for the differential effects of recruitment strategies by putative confounding or modifying factors in the dataset. Other variables related to pre-treatment beliefs (expectancies) and attitudes (readiness to change or motivation) may explain the differences between the patients recruited by these two strategies. Unfortunately, more detailed information on attitudes was lacking in this trial, though recent studies suggest that these factors might play important roles in this context (Goossens et al 2005, Jensen et al 2004, Keefe et al 2004).

Blinding

As a consequence of the pragmatic design of the trial, patients and health care providers could not be blinded, though the persons assessing the outcome measures and analysing the data were unaware of treatment allocation. The fact that patients were not blinded may have introduced withdrawal bias. However, results showed that the numbers of patients who withdrew because of the nature of the interventions (frequency of treatment sessions and treatment preferences) were small and similar for both groups (2 GET versus 3 UC). Furthermore, the lack of blinding may have caused treatment preferences to influence the results of the trial (van Schaik et al 2004, Thomas et al 2004, van der Windt et al 2000). However, treatment preferences were found to have no influence on the effectiveness of treatments in this trial. Since no more than 5% of the patients in this study had prior experiences with behavioural treatments and 82% had no clear preference on this intervention, we consider that treatment preferences were less likely to have influenced the results in this study. We learn from this study that treatment preferences are probably more involved in unblinded studies in which participants have more explicit treatment preferences.

Contamination

The content of the treatments received by patients allocated to GET and usual care showed that none of the patients allocated to GET were treated with usual care physiotherapy during the treatment period. By contrast, 19 patients allocated to usual care were treated by a physiotherapist, but none of these were treated with behavioural therapy as such. Since the principles of the biopsychosocial model are nowadays more commonly applied in usual care, the differences between treatments might have become less distinct than intended. Earlier studies focused on the interaction between health care providers and pain patients and found that health care providers' attitudes and beliefs influenced their recommendations regarding activities for patients with chronic low back pain (Rainville et al 1995, Linton 2002). Health care providers seemed to be either more behaviourally oriented or more biomedically oriented, and physiotherapists who had attended a biopsychosocial education course proved to be more behaviourally oriented (Ostelo et al 2003). Furthermore, behavioural or biomedical orientation among physiotherapists was associated with perceived harmfulness of physical activities and recommendations for return to work (Houben et al 2005). Further research is needed to explore the influence of attitudes and beliefs among health care providers in trials.

Evaluation of the intervention process

The process evaluation is of utmost importance in studies on clinical effectiveness: first, to know whether the treatment under study was performed according to protocol, second, to know whether the treatment is feasible in normal practice, and third, to identify any need to improve the protocol to facilitate its implementation. Chapter 6 describes a process evaluation of GET. Patients and physiotherapists were involved in the development and evaluation of GET, as this would stimulate the implementation of the programme. Nevertheless, three comments should be made on the methods used in the present process evaluation. First, since indirect methods were used, based only on reports, no evidence is available of what actually happened during the treatment sessions. Second, since the physiotherapists and the patients were involved in the assessments, scores might be flawed. Third, reports on the quantitative application of the programme do not provide information about the quality of its application.

Outcome measures

The outcome measures of this study might be critically considered. Firstly, there is at present no consensus on the outcome that is the most appropriate for shoulder complaints (Green et al 2000). In the 'main complaints' instrument, patients were asked at baseline to select three daily activities they regarded as most important in relation to their shoulder complaints, but not necessarily related specifically to pain. Since activities, and their relevance or importance in daily life, can vary widely between patients with shoulder complaints, and the GET programme is tailored to the patient's goals and needs, this measure is considered to be appropriate to assess the performance of daily activities in this trial.

Secondly, some outcome measures used in this trial turned out to be inappropriate. At the level of participation, we assessed sick leave and generic health-related quality of life. Only 56% of all participants reported having paid work at baseline, and only 8% of all patients with paid work reported having been on sick leave from paid work. The margin for improvement as regards to sick leave from paid work was relatively small, and given the small numbers of patients with paid work, the trial had insufficient power to yield feasible data on 'return to work'.

Generic health-related quality of life was rated on the EQ5D (Brooks 1996) to enable the outcomes to be compared with those of other trials in terms of effectiveness and cost-effectiveness. The EQ5D consists of a descriptive system for health status, related to five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale. However, this measure turned out not to be sensitive enough to detect changes in both treatment groups. It is very likely that improvements in individual daily activities were too specific to be detected by this generic health-related quality of life measure. These findings on the lack of responsiveness of the EQ5D are comparable with those of earlier studies on musculoskeletal disorders (Dawson et al 2001, Marra et al 2005). We suggest that future cost-effectiveness studies on musculoskeletal disorders should use more responsive quality of life instruments (e.g., the Medical Outcome Study Short-Form (SF-36) Health Survey) and incremental cost-effectiveness ratios of disease-specific instruments (e.g., the 'main complaints' instrument or perceived recovery), to enable generalisation of outcomes.

A final comment on outcome measures relates to the strengths and weaknesses of the outcomes used. This trial was embedded in a research programme on shoulder complaints,

including a comprehensive prognostic cohort study with three trials in subcohorts. The strength of this programme is the ability to pool the outcomes of the subcohort trials. A weakness might be a lack of outcome measures relevant to subcohorts. Unfortunately, pre-treatment attitudes (readiness to change, motivation) and beliefs (expectancies) on pain and pain disability were not assessed in the present trial. As was also mentioned above, we consider these outcome measures worthwhile as a means to explore in more detail the behavioural changes we found in patients with chronic shoulder complaints.

Explorative analyses

Further comments should be made on the explorative analyses in this trial. Patients allocated to GET showed statistically significantly higher scores for improvement on pain-catastrophising, kinesiophobia and pain-related fear. Since GET is an operant-behavioural treatment (and not a cognitive treatment), it could be assumed that patients gradually learned from positive experiences in performing daily activities during treatment and their improved performances contributed to a reduction of pain-catastrophising, kinesiophobia and pain-related fear in the long term. This interpretation is in line with those of earlier studies of chronic low back pain patients, in which pain-catastrophising, pain-anxiety and pain-related fear were associated with the lack of performance of activities through over-predicting actual pain and under-predicting abilities to perform physical tasks and to adjust pain behaviour (Vlaeyen and Linton 2000, Keefe et al 2004).

IMPLICATIONS AND RECOMMENDATIONS FOR CLINICAL PRACTICE AND FUTURE RESEARCH

From health care perspective

The present study shows that GET is more effective than UC in restoring the performance of daily activities in patients with chronic shoulder complaints in primary care and reduces direct health care costs and direct non-health care costs, although beneficial effects are small. Based on these results, it is recommended to use GET to restore daily activities in patients with chronic shoulder complaints in primary health care.

Beneficial effects of GET are greater in patients with prolonged pain. Predicting which patients are at risk of persistent shoulder pain in the long term in primary care is of great interest if we want to achieve a better match between the GET programme and patient characteristics. Recently, high pain intensity at onset was found to be a consistent predictor of prolonged pain in patients with shoulder complaints in primary care (Kuipers et al 2004). Therefore, we recommend the use of the GET programme in patients with more severe shoulder pain at onset.

The study has also shown that beneficial effects are smaller in patients showing a painful arc during physical examination. Painful arc is a well-known sign associated with sub-acromial impingement, as the initial stage of rotator cuff injuries, with rotator cuff tears as the final stage (Neer and Welsh 1977, Pyne 2004). No recommendations can be given to either support or refute the use of GET in patients showing a painful arc. We recommend more research on the phenomenon of painful arc, to elucidate the value of exercise programmes in general for patients with shoulder impingement in primary care.

Furthermore, this study shows that GET is effective in restoring daily activities in patients with chronic shoulder complaints in long term in a primary care setting and might as such

prevent more intensive and more expensive multidisciplinary treatment of these patients in secondary or tertiary care settings. .

GET reduced direct health care costs and direct non-health care costs in patients with chronic shoulder complaints, although total costs for GET were higher due to higher programme costs. We recommend that the programme should focus more on work-related goals and work-related activities in patients having paid work, which might improve the social benefits of GET.

GET fits well into developments in primary care physiotherapy in the Netherlands in which consultation of a primary care physiotherapist for (graded exercise) group therapy was introduced only recently and is paid for by Dutch health insurance companies.

We recommend revision of the practice guidelines for shoulder complaints of the Dutch College of General Practitioners. We suggest that the GET programme should be considered as an effective treatment in restoring activities in patients with chronic shoulder complaints in the long term, predominantly in patients with severe pain at onset.

From patient's perspective

From a patient's point of view, this study shows that patients with chronic shoulder complaints can derive short- and long-term benefit from GET in terms of improved performance of daily activities. The GET programme is 'personality'-based, in that it is tailored to patients' individual needs in terms of treatment goals and levels of activity, and focuses on patients' behaviour to meet these goals and improve their activities. We recommend that patients should be very explicit in defining the treatment goals and should be well aware that the programme does not primarily aim to reduce pain. This requires a clear explanation to the patients before starting the treatment.

GET fits well into the policy trend to put the patients' preferences as the start of the treatment in non acute situations. Furthermore, GET fits well into the trend towards acceptance-based treatments in patients with chronic pain, in which the focus is not on reducing pain but on reducing the distressing and the disabling influence of pain in chronic pain patients (Mc Cracken et al 2005) .

From providers' perspective

From the point of view of practitioners, education and training of health care providers, this study shows that GET can be administered successfully in a primary health care setting by physiotherapists. Implementation of GET could be promoted if it is embedded in a multidisciplinary biopsychosocial approach of health care providers on shoulder complaints in primary care. Since attitudes and beliefs of health care providers correlate with their recommendation about activities, special attention should be paid to these attitudes. More research is needed into the interactions between health care providers and patients with shoulder complaints, to elucidate the mechanisms involved in treatments.

From research perspective

Further research is needed to optimise the effectiveness of behavioural treatment in patients with chronic shoulder complaints. More research is needed on the cognitive and behavioural aspects of pain prediction in patients with chronic shoulder pain at the onset of complaints, as it could provide new insights into the prognosis and course of complaints. We assumed the GET programme most suitable for patients with discrepant pain behaviour and pain beliefs,

who might either postpone activities because they believe activity may cause damage or re-injury, or ignore the pain and consequently exceed suitable levels of activity. More research is needed to explore the beneficial effects of GET in “avoiders” and “overusers”.

More research is also needed on the specific biobehavioural mechanisms for the transition from acute to chronic pain and disability in patients with shoulder complaints to optimise treatment. Recent developments in behavioural pain research, focussing in greater detail on pain-related fear in chronic pain patients, have shown that education and exposure in vivo, with behavioural experiments for patients who report fear of movement/(re)injury, might be more effective than gradual operant learning in terms of reducing pain-related fear and improving the performance of daily activities (de Jong et al 2005). Since GET asks patients to select specific relevant daily activities, this might exclude activities they have been avoiding for a long time. In exposure in vivo, patients are exposed to these threatening activities, leading directly to fear-reduction. More research is needed to elucidate whether or not the operant-behavioural GET programme administered by a physiotherapist should be applied or combined with education and exposure administered by a psychologist in highly fearful patients with shoulder complaints in primary care.

Finally, we consider process evaluation to be of the utmost importance in future studies of clinical effectiveness and recommend the development of measurement instruments to evaluate intervention processes and report on process evaluations in trials and on implications for clinical effectiveness and clinical practice.

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Summary

Samenvatting

SUMMARY

This thesis reports on a study of the clinical effectiveness and cost-effectiveness of a behavioural Graded Exercise Therapy (GET) programme for patients with chronic shoulder complaints in a primary care setting. Shoulder complaints are serious musculoskeletal problems in view of their occurrence, course and persistence. Shoulder complaints manifest themselves as pain and limitations in the performance of daily activities. At present, there is limited evidence that commonly applied interventions for shoulder complaints speed up recovery in the short term, though there is no or conflicting evidence on long-term effects of conservative treatments. Behavioural treatments have proved to be effective mostly for chronic low back pain patients and in multidisciplinary settings. We assumed that behavioural treatment might be an effective means of optimising the course of chronic shoulder complaints in a primary care setting as well. We therefore initiated a randomised clinical trial to compare the clinical effectiveness and cost-effectiveness of a behavioural Graded Exercise Therapy programme with usual care in patients with chronic shoulder complaints.

Chapter 1 reports on the personal and economic burden imposed by shoulder complaints, on the lack of evidence about the aetiology, prognosis and management of shoulder complaints, and on the need to optimise treatment. It also presents the objectives of the research project described in this thesis. It has been estimated that about 40% of all patients who visit their general practitioner with a new episode of shoulder complaints endure complaints for up to 12 months. Musculoskeletal disorders, of which shoulder complaints constitute the second largest group after low back pain, account for the second largest share in healthcare costs in the Netherlands. At present, it is unclear what factors contribute to the initiation of shoulder complaints, what factors are involved in the transition from acute to chronic complaints or what factors play a role in the persistence of chronic complaints. However, there is general agreement that psychological factors are involved in the course of chronic pain. A behavioural Graded Exercise Therapy (GET) programme was developed to optimise the course and to reduce healthcare costs for patients with chronic shoulder complaints in primary care. The main objective of the studies reported on in this thesis was to evaluate the short-term and long-term clinical effectiveness and the cost-effectiveness of the GET programme in terms of restoring the performance of daily activities by patients with chronic shoulder complaints, compared with usual care in a primary care setting. We also evaluated the intervention process and the feasibility of the newly developed GET programme in a primary care setting. Finally, we evaluated whether the use of two recruitment strategies in this trial had influenced its outcomes.

Chapter 2 describes the concepts and the development of the GET programme and the design of the pragmatic randomised clinical trial to evaluate its clinical effectiveness and cost-effectiveness. The chapter focuses on the reconceptualisation of pain in research and practice during the past decades and the development of a new biopsychosocial model, which assumes that biological, psychological and social factors might be involved in the persistence or reduction of chronic pain. It describes the operant conditioning principles for the management of chronic pain and the way in which pain behaviour and pain-related inactivity are acquired and can be modified by changing the consequences of this behaviour. Furthermore, it discusses the content and the main components (graded activity, time contingency and operant conditioning) of the GET programme and the content of the

Guidelines for Shoulder Complaints of the Dutch College of General Practitioners (wait-and-see policy, possibly supplemented with analgesics and NSAIDs, corticosteroid injections and referral to physiotherapy, which is considered in complaints persisting for six weeks or more). Finally, it presents the design of this pragmatic randomised clinical trial, including the methods and the statistical analyses.

Chapter 3 presents short-term results on the clinical effectiveness of the GET programme. A total of 176 patients were randomised and allocated either to GET ($N=87$) or usual care ($N=89$). The short-term effects were assessed after 12 weeks of treatment. Primary outcome measures were the Main Complaints instrument and the Shoulder Disability Questionnaire (SDQ). The secondary outcome measures included shoulder pain scored on the Shoulder Pain Scores (SPS), perceived recovery measured on an eight-point ordinal scale (0 fully recovered – 7 very much deteriorated), generic health-related quality of life rated on the EQ-5D, catastrophising, coping with pain, internal locus of control and external locus of control as assessed by the Pain Coping and Cognition List (PCCL), kinesiophobia rated on 2 items of the Tampa Scale for Kinesiophobia (TSK) and fear-avoidance beliefs scored on the subscale of fear-avoidance beliefs about physical activity, adjusted for SC, of the Fear-Avoidance Beliefs Questionnaire (FABQ-DV). GET led to a larger improvement in the performance of daily activities than usual care. However, only the mean differences between groups in the performance of activities related to the main complaints reached statistical significance ($P=0.049$, 95% CI: 0.0, 15.0). The observed beneficial effects were considered to be small (calculated effect sizes: 0.30 for the Main Complaints instrument and 0.07 for the SDQ). Subgroup analysis showed greater improvements in the mean scores on the Main Complaints instrument for patients not reporting pain reduction over time. GET seemed to be just as effective as usual care in restoring the performance of daily activities, as assessed by the SDQ, in patients showing a painful arc during physical examination. We concluded that GET is more effective than usual care in restoring the performance of daily activities in patients with chronic shoulder complaints in the short term, although beneficial effects at the end of the treatment period were small.

Chapter 4 presents long-term results on the clinical effectiveness of GET. These effects were assessed after 26 and 52 weeks. GET showed statistically significantly greater improvements than usual care on the Main Complaints instrument immediately after 12 weeks of treatment, and these improvements lasted for at least 52 weeks ($P=0.025$, 95% CI: 1.2, 17.3). GET was equally effective as usual care in patients with a painful arc during physical examination and more effective than usual care in patients with no pain reduction during the treatment period. Statistically significantly greater improvements with GET were found for catastrophising at 12 weeks ($P=0.028$, 95% CI: 0.0, 0.4) and for fear avoidance beliefs ($P=0.043$, 95% CI: 0.0, 0.8) and kinesiophobia ($P=0.003$, 95% CI: 0.3, 1.3) at 52 weeks. Calculated effect sizes were rather modest (up to 0.45). We concluded that the effectiveness of GET compared with usual care in restoring daily activities in patients with chronic shoulder complaints, as assessed immediately after treatment, persists in the long term (at least 52 weeks), although clinical benefits are rather modest.

Chapter 5 presents results of the cost-effectiveness study that was performed alongside the randomised clinical trial. Clinical outcomes (main complaints, shoulder disability (SDQ) and

generic health-related quality of life (EQ5D)) and costs (intervention costs, direct health care costs, direct non-health related costs and indirect costs) were assessed during the 12-week treatment period and during 52 weeks of follow-up. Results showed that GET significantly reduced direct health care costs ($p=0.000$) and direct non-health care costs ($p=0.029$) in these patients. Nevertheless, total costs during the one-year follow-up period were significantly higher ($p=0.001$; € 530 for GET versus € 377 for UC) due to the higher costs of the intervention. Incremental cost-effectiveness ratios for the severity of the main complaints (0 – 100), SDQ (0 – 100) and EQ5D (-1.0 – 1.0) were € 17, € 74, and € 5278 per unit of improvement, respectively. We conclude that GET is more effective than usual care in the short and long term and reduces direct health care costs and direct non-health care costs, but is associated with higher costs of the intervention itself.

Chapter 6 reports on the evaluation of the intervention process. This process evaluation was done for three reasons: first, to know whether the programme had been administered as planned, second, to know whether this treatment would be feasible in normal practice, and third, to identify the need for improvements to the protocol to facilitate its implication. We evaluated the degree to which the programme had been applied according to protocol, patient adherence to the programme, and the suitability of the programme according to patients and physiotherapists. Twenty participating physiotherapists and 87 patients allocated to GET were asked to evaluate the intervention process. Furthermore, a sample of 10 patients, taken from the total number of 87 patients allocated to GET, were invited to take part in a focus group interview at the end of the study. We evaluated the intervention process using a treatment registration form filled in by the physiotherapists during treatment, evaluation forms filled in independently by physiotherapists and patients after the treatment period, and information gathered during the focus group interview at the end of the study.

Results showed that GET had been applied according to protocol to an acceptable degree, and participating patients showed satisfactory adherence to the programme. The programme could be improved in terms of the goal-setting process, and the implementation of GET could be facilitated by embedding the programme in a multidisciplinary approach in primary care. We conclude that the clinical effectiveness of GET in this trial was not influenced by flaws in the administration of the programme or by lack of patient adherence.

Chapter 7 reports on an evaluation of the use of two recruitment strategies in this trial. Since the numbers of patients recruited during general practitioner consultations for chronic shoulder complaints were smaller than expected, subjects were also invited to enrol by means of advertisements in a local newspaper. Patients recruited by their general practitioners were compared with those recruited by advertisement as regards baseline characteristics, withdrawal (drop-outs and losses to follow-up) and post-treatment clinical outcomes. Results showed that patients recruited by the general practitioners ($N=83$) were similar to those recruited by advertisement ($N=93$) in terms of demographic characteristics and clinical outcome measures at baseline, but differed slightly in disease characteristics and treatment preferences. Recruitment strategy was not related to reasons for withdrawal or numbers of withdrawals. Improvements on outcome measures were greater in patients recruited by the general practitioners, irrespective of allocated treatment. Results on the clinical effectiveness of treatments at the end of the treatment period or during follow-up were neither modified by recruitment strategy, nor by differences between the two strategy groups in patient

characteristics found at baseline. We concluded that using two recruitment strategies did not influence the trial's clinical effectiveness outcomes. However, recruitment strategy should be regarded as a putative modifying factor in the design of a study.

Chapter 8 presents a general discussion, focussing on the answers to the research questions presented in the first chapter. It reviews the main findings of the randomised clinical trial, and deals with some general methodological and practical issues concerning the study, including the recruitment of patients and the evaluation of the intervention process. Finally, it presents some implications of this trial for clinical practice and future research.

SAMENVATTING

Dit proefschrift gaat over een studie naar de klinische effectiviteit en de kosteneffectiviteit van een gedragsmatig Graded Exercise Therapy (GET) programma voor patiënten met chronische schouderklachten in de eerste lijn. Schouderklachten vormen een omvangrijk gezondheidsprobleem door het vóórkomen, het beloop en het aanhoudende karakter ervan. Schouderklachten worden gekenmerkt door pijn en door beperkingen in het uitvoeren van dagelijkse activiteiten. Op dit moment is de bewijskracht dat de gebruikelijke behandelingen voor schouderklachten het herstel bespoedigen beperkt en er is geen of tegengesteld bewijs dat deze behandelingen effectief zijn op de lange termijn. Gedragsmatige behandelingen blijken effectief te zijn in de behandeling van patiënten met lage rugklachten in een multidisciplinaire setting. Wij veronderstelden dat een gedragsmatige behandeling tevens effectief zou kunnen zijn in het verbeteren van dagelijkse activiteiten bij patiënten met chronische schouderklachten in de eerste lijn. Daarom hebben we in een pragmatische gerandomiseerde studie, de klinische effectiviteit en de kosteneffectiviteit van een gedragsmatig Graded Exercise Therapy programma vergeleken met die van de standaard behandeling voor schouderklachten (conform de Standaard Schouderklachten van het Nederlands Huisartsengenootschap) bij patiënten met chronische schouderklachten in de eerste lijn.

Hoofdstuk 1 beschrijft allereerst, de persoonlijke hinder die patiënten met schouderklachten ondervinden en de economische en maatschappelijke gevolgen van schouderproblematiek. Verder wordt ingegaan op het gebrek aan bewijs over het ontstaan, de prognose en de behandeling van schouderklachten en de behoefte om de behandeling voor schouderklachten verder te verbeteren. Ten slotte worden de onderzoeksvragen die in dit proefschrift aan bod komen gepresenteerd.

Circa 40% procent van alle patiënten die voor een nieuwe episode van schouderklachten de huisarts bezoekt, heeft na 12 maanden nog restklachten. Schouderklachten vormen na lage rugklachten de op één na grootste groep van klachten van het bewegingsapparaat. Klachten van het bewegingsapparaat nemen in Nederland het op één na grootst aandeel in de kosten voor gezondheidszorg voor haar rekening. Op dit moment is nog onduidelijk welke factoren betrokken zijn bij het ontstaan van schouderklachten, welke factoren betrokken zijn bij de overgang van acute naar chronische klachten of welke factoren een rol spelen bij het voortbestaan van chronische schouderklachten. Echter, er is consensus dat psychologische factoren betrokken kunnen zijn bij het beloop van chronische pijnklachten van het bewegingsapparaat. Daarom werd een gedragsmatig GET programma ontwikkeld voor patiënten met chronische schouderklachten in de eerste lijn met het doel het activiteitsniveau voor deze patiënten te verbeteren en de gezondheidskosten te verminderen. In deze studie zijn de klinische effectiviteit en de kosteneffectiviteit van GET, in het verbeteren van dagelijkse schouderactiviteiten op de korte en de lange termijn bij patiënten met chronische schouderklachten in de eerste lijn, vergeleken met die van de standaard behandeling. Verder werd het behandelproces geëvalueerd en de uitvoerbaarheid van het nieuw ontwikkelde GET programma in een eerste lijn setting onderzocht. Tot slot hebben we onderzocht of het gebruik van twee strategieën om patiënten te werven voor deelname aan deze studie, de resultaten van deze trial heeft beïnvloed.

Hoofdstuk 2 beschrijft de achtergronden en de ontwikkeling van het GET programma en het ontwerp van dit pragmatisch gerandomiseerd klinisch onderzoek waarin de klinische

effectiviteit en de kosteneffectiviteit van dit programma zijn onderzocht. Het gaat in op de veranderde opvattingen over pijn in onderzoek en praktijk gedurende de laatste decennia en de ontwikkeling van een nieuw biopsychosociaal model, waarin biologische, psychologische en sociale factoren betrokken kunnen zijn bij het voortbestaan of bij het verminderen van chronische pijnklachten. Het beschrijft de principes van operante conditionering in de behandeling van chronisch pijn en de wijze waarop pijngedrag en inactiviteit door pijn aangeleerd zijn en gemodificeerd kunnen worden door het veranderen van de consequenties van dit gedrag. Verder wordt de inhoud en de belangrijkste elementen (gradueel oefenen, tijdcontingentie en operante conditionering) van het GET programma en de inhoud van de Standaard Schouderklachten van het Nederlands Huisartsengenootschap (afwachting beleid, eventueel aangevuld met pijnstillers of NSAID's, corticosteroid injecties en verwijzing naar de fysiotherapeut, dat overwogen wordt bij langer dan 6 weken bestaande klachten) besproken. Tot slot wordt het ontwerp van dit pragmatisch gerandomiseerd klinisch onderzoek, inclusief de methoden en de statistische analyses, gepresenteerd.

Hoofdstuk 3 beschrijft de klinische effectiviteit van het GET programma op de korte termijn. Honderdzesenzeventig patiënten werden gerandomiseerd en toegewezen aan GET (N=87) of aan de standaard behandeling (N=89). De korte termijn resultaten werden direct na afloop van de 12 weken durende behandeling bepaald. De belangrijkste uitkomstmaten waren de Patiënt Specifieke Klacht (PSK) en de Shoulder Disability Questionnaire (SDQ). Overige uitkomstmaten waren schouderpijn, gescoord op de Shoulder Pain Score (SPS), ervaren herstel, gemeten op een acht-punten ordinale schaal (0 volledig herstel – 8 zeer veel verslechterd), kwaliteit van leven, gemeten met de EQ5D, catastrofen, pijn coping, interne pijnbeheersing en externe pijnbeheersing, gemeten met de Pain Coping and Cognition List (PCCL), kinesiofobie, gemeten met de Tampa Scale for Kinesiophobia (TSK), en pijn-gerelateerde vrees, gemeten met de subschaal pijngerelateerd vrees voor fysieke activiteiten van de Fear-Avoidance Beliefs Questionnaire (FABQ). GET liet een grotere vooruitgang zien in het uitvoeren van dagelijkse schouder activiteiten dan de standaard behandeling voor schouderklachten. Echter, alleen de verschillen tussen de beide groepen gemeten met de PSK waren statistisch significant ($P=0.049$, 95% BI: 0.0, 15.0). De omvang van de verschillen tussen de groepen waren klinisch gezien klein (berekende effectsizes: 0.30 voor de PSK en 0.07 voor de SDQ). Subgroepanalyses lieten een grotere vooruitgang zien op de PSK voor patiënten waarin de pijn in de loop van de tijd niet was verminderd. GET is even effectief in het verhogen van dagelijkse schouderactiviteiten gemeten met de SDQ bij patiënten die tijdens het lichamelijk onderzoek een pain-ful arc vertoonden. Wij concludeerden dat GET op de korte termijn effectiever is dan de standaard behandeling in het verhogen van dagelijkse activiteiten bij patiënten met chronische schouderklachten, ook al zijn de waargenomen verschillen in klinisch opzicht klein.

Hoofdstuk 4 beschrijft de effectiviteit van GET op de lange-termijn. Deze effecten werden gemeten na 26 en 52 weken. GET liet statistisch significant grotere verschillen zien dan de standaard behandeling op de PSK direct na afloop van de behandeling en deze verschillen bleefden op zijn minst voor de periode tot 52 weken ($P=0.025$, 95% BI: 1.2, 17.3). GET was even effectief als de standaard behandeling voor patiënten met een pain-ful arc tijdens het lichamelijk onderzoek en effectiever dan de gebruikelijke behandeling voor patiënten die geen pijnvermindering in de loop van de tijd lieten zien. Statistisch significant grotere

verschillen voor GET werden gezien voor catastrofen na 12 weken ($P=0.028$, 95% BI: 0.0, 0.4) en voor pijngerelateerde vrees ($P=0.043$, 95% BI: 0.0, 0.8) en kinesiofobie ($P=0.003$, 95% BI: 0.3, 1.3) na 52 weken. De berekende effectsizes waren bescheiden (tot 0.45). We concludeerden dat de grotere effecten van GET, vergeleken met de standaard behandeling, op het verhogen van dagelijkse activiteiten bij patiënten met chronische schouderklachten gemeten direct na afloop van de 12 weken durende behandeling, beklijven op de lange termijn na 52 weken, ook al zijn de verschillen klinische gezien bescheiden.

Hoofdstuk 5 beschrijft de resultaten van de kosteneffectiviteit studie die parallel aan het gerandomiseerd klinisch onderzoek werd uitgevoerd. Klinische uitkomstmaten (PSK, SDQ en EQ5D) en kosten (interventiekosten, directe gezondheidsgerelateerde kosten, directe niet-gezondheidsgerelateerde kosten en indirecte kosten) werden gemeten gedurende de 12 weken durende behandelperiode en gedurende de follow-up periode tot 52 weken. De resultaten lieten zien dat de directe gezondheidsgerelateerde kosten ($P=0.000$) en de directe niet-gezondheidsgerelateerde kosten ($P=0.029$) voor GET patiënten statistisch significant verminderden. Desondanks waren de totale kosten gedurende de 52 weken follow-up periode significant hoger ($P=0.001$; € 530 voor GET tegen € 377 voor de standaard behandeling) door de hogere kosten voor de interventie. De kosten-effectiviteitsratio's voor de PSK (0-100), de SDQ (0-100) en de EQ-5D (-1.00 - 1.00) bedragen respectievelijk € 17, € 74 en € 5278 per eenheid verbetering. We concludeerden dat GET effectiever is in het verbeteren van dagelijkse activiteiten op de korte en lange termijn en GET de directe gezondheidsgerelateerde kosten en directe niet-gezondheidsgerelateerde kosten voor patiënten met chronische schouderklachten verminderd, maar geassocieerd is met hogere interventiekosten.

Hoofdstuk 6 beschrijft de resultaten van het onderzoek naar het interventie proces. Deze procesevaluatie werd uitgevoerd om drie redenen: ten eerste, om te onderzoeken of het programma is uitgevoerd zoals gepland, ten tweede, om te onderzoeken of het programma uitvoerbaar is in de dagelijkse praktijk, ten derde, om te onderzoeken op welke punten het programma verbeterd kan worden om de implementatie ervan te faciliteren. We hebben onderzocht in hoeverre het programma is uitgevoerd volgens het behandelprotocol, de patiënten trouw waren aan het programma en de patiënten en fysiotherapeuten het programma geschikt vonden voor de behandeling van iedere patiënt afzonderlijk. De 20 deelnemende fysiotherapeuten en de 87 patiënten die werden toegewezen aan GET, werden gevraagd het behandelproces te evalueren. Verder werd een steekproef van 10 patiënten, genomen uit de 87 patiënten die werden toegewezen aan GET, uitgenodigd voor deelname aan een focusgroep interview na afloop van de studie. Het behandelproces werd geëvalueerd aan de hand van de behandelverslagen ingevuld door de fysiotherapeuten gedurende de behandelperiode, aan de hand van de evaluatieformulieren die de patiënten en de fysiotherapeuten onafhankelijk van elkaar hebben ingevuld na afloop van de behandelperiode en aan de hand van de informatie verzameld tijdens het focusgroep interview aan het eind van de studie. De resultaten lieten zien dat GET op een acceptabel niveau is uitgevoerd volgens het behandelprotocol en de deelnemende patiënten voldoende trouw waren aan het programma. Het GET programma kan verbeterd worden met betrekking tot het proces van het stellen van de behandeldoelen en de implementatie van GET kan gefaciliteerd worden als het programma ingebed zou worden in een multidisciplinaire benadering van patiënten met chronische schouderklachten in de eerste lijn. We concludeerden dat klinische

effectiviteit van het GET programma in deze studie niet beïnvloed is door onvolkomenheden in de uitvoering van het programma of door gebrek aan therapietrouw onder de deelnemende patiënten.

Hoofdstuk 7 beschrijft het onderzoek naar de toepassing van twee strategieën voor de werving van patiënten in deze studie. Omdat het aantal patiënten, gerekruteerd door de huisarts tijdens het bezoek aan de praktijk voor schouderklachten, geringer was dan verwacht, werden tevens patiënten met chronische schouderklachten uitgenodigd voor deelname aan de studie via een advertentie in een plaatselijk nieuwsblad. Patiënten gerekruteerd door de huisarts en patiënten gerekruteerd via advertenties werden met elkaar vergeleken met betrekking tot de karakteristieken van de patiënten gemeten bij het vooronderzoek, het aantal uitvallers tijdens de studie en gedurende de follow-up periode en met betrekking tot de klinische uitkomstmaten na de behandeling. Resultaten lieten tijdens het vooronderzoek geen verschillen zien tussen de patiënten gerekruteerd via de huisarts (N=83) en patiënten gerekruteerd via advertenties (N=93) met betrekking tot demografische factoren en klinische uitkomstmaten en slechts geringe verschillen met betrekking tot ziektekenmerken en behandelvoorkeuren. Wervingstrategie was niet gerelateerd aan het aantal uitvallers of aan de redenen voor uitval in deze studie. Patiënten gerekruteerd via de huisarts lieten een grotere vooruitgang zien op de belangrijkste klinische uitkomstmaten, ongeacht de behandeling waaraan patiënten werden toegewezen. De resultaten op de belangrijkste klinische uitkomstmaten werden niet gemodificeerd door wervingstrategie of door de gevonden verschillen tussen de groepen bij het vooronderzoek. We concludeerden dat het gebruik van twee wervingsstrategieën de resultaten op de belangrijkste uitkomstmaten in deze studie niet heeft beïnvloed. Echter, wervingstrategie moet beschouwd worden als een mogelijke effectmodificator in het ontwerp van een studie.

Hoofdstuk 8 gaat in op de antwoorden op de onderzoeksvragen zoals beschreven in het eerste hoofdstuk. Het beschrijft de belangrijkste resultaten van dit gerandomiseerd klinisch onderzoek. Verder komen enkele methodologische en praktische aspecten met betrekking tot de uitvoering van deze studie aan bod, zoals de werving van patiënten en de procesevaluatie. Tot slot worden de implicaties voor de klinische praktijk and voor verder onderzoek beschreven.

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DANKWOORD

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Curriculum Vitae

De Gele Keizer was zo maar op reis
ten noorden van het Rode Water,
bij de berg Kwen Loen.
Hij keek over de rand van de Wereld.
Op weg naar huis verloor hij zijn donkere parel.
Hij stuurde Wetenschap uit
om de parel te vinden:
maar deze vond hem niet.
Hij stuurde Onderzoek uit
om de parel te vinden:
maar deze vond hem niet.
Hij stuurde Logica uit
om de parel te vinden:
maar deze vond hem niet.
Toen vroeg hij het aan Niets –
en Niets had hem!

Daarop zei de Gele Keizer:
"Is dat niet merkwaardig:
Niets werd niet uitgestuurd
En hij deed niets om de parel te vinden;
Maar hij had hem!"
(T'wang-tseu)

ABOUT THE AUTHOR

Jacques Geraets was born on November 9, 1958 in Brunssum, the Netherlands. After he obtained his VWO diploma at the St.Janslyceum in Hoensbroek, he studied Physiotherapy at the Akademie voor Fysiotherapie in Heerlen and graduated in 1983. Subsequently, he studied Traditional Chinese Medicine at the International Free University in Maastricht/Basel. Since 1983 he has been working as a Primary Care Physiotherapist in Landgraaf. He started his study in Health Sciences at Maastricht University in 1995. He specialised in Movement Science and graduated in 1998. His master's thesis focused on the accuracy and reliability of shouldersonography. Since 1999 he is engaged in teaching methodology in the post-HBO training courses Sports Physiotherapy and Manual Therapy at the Hogeschool van Utrecht. In 2002 he was registered as an epidemiologist. Since 2001 he combined his work as a Physiotherapist with his PhD-project as described in this thesis at the department of General Practice of Maastricht University and the Institute for Rehabilitation Research iRv in Hoensbroek. The studies presented here are embedded in a research programme of the Netherlands Organisation for Scientific Research, including a comprehensive prognostic cohort study on shoulder complaints in primary care, with three randomised clinical trials on the clinical-effectiveness and cost-effectiveness of three treatment modalities in subcohorts. In March 2006, Jacques will also start teaching at the Hogeschool Zuyd in Heerlen. He is married to Reinilde Breuer and father of Maarten, Anouk, Jasper and Malou.

List of publications

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